IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF OHIO
EASTERN DIVISION

MDL NO. 2804
CASE NO. 17-md-2804
Hon. Dan A. Polster

IN RE: NATIONAL PRESCRIPTION OPIATE LITIGATION

THIS DOCUMENT RELATES TO:
TRACK THREE CASES

REMOTE VIDEO DEPOSITION OF KATHERINE KEYES, PH.D.

June 3, 2021

REPORTED BY: Laura H. Nichols
Certified Realtime Reporter,
Registered Professional
Reporter and Notary Public

A P P E A R A N C E S

(All Appearing Remotely)

FOR THE PLAINTIFFS:

Messrs. Donald C. Arbitblit
Ian Bensberg, Britt Cibulka
and Matias Bustamante
Attorneys at Law
Lieff Cabraser Heimann & Bernstein, LLP
275 Battery Street, 29th Floor
San Francisco, California 94111-3339
(415) 956-1000
darbitblit@lchb.com
ibensberg@lchb.com
mbustamante@lchb.com
bcibulka@lchb.com

-and-

Ms. Paulina do Amaral
Attorney at Law
Lieff Cabraser Heimann & Bernstein, LLP
250 Hudson Street
Eighth Floor
New York, New York 10013
(212) 355.9500
pdoamaral@lchb.com

A P P E A R A N C E S (Continuing)

(All Appearing Remotely)

ALSO FOR THE PLAINTIFFS:

Mr. Peter H. Weinberger
Attorney at Law
Spangenberg Shibley & Liber LLP
1001 Lakeside Avenue East
Suite 1700
Cleveland, Ohio 44114
(216) 600-0114
pweinberger@spanglaw.com

ALSO FOR THE PLAINTIFFS:

Ms. Jo Anna Pollock
Attorney at Law
Simmons Hanly Conroy
One Court Street
Alton, Illinois 62002
jpollock@simmonsfirm.com
(618) 693-3104

A P P E A R A N C E S (Continuing)

(All Appearing Remotely)

FOR THE DEFENDANT, RITE AID:

Ms. Elizabeth I. Buechner
Attorney at Law
Morgan, Lewis & Bockius LLP
101 Park Avenue
New York, New York 10178-0060
(212) 309-6000
elizabeth.buechner@morganlewis.com

FOR THE DEFENDANT, WALGREENS BOOTS ALLIANCE, INC.; WALGREEN CO.; AND WALGREEN EASTERN CO., INC.:

Mr. Kaspar Stoffelmayr
Attorney at Law
Bartlit Beck
Courthouse Place
54 West Hubbard Street
Chicago, Illinois 60654
(312) 494-4400
kaspar.stoffelmayr@bartlitbeck.com

A P P E A R A N C E S (Continuing)

(All Appearing Remotely)

FOR THE DEFENDANT, WALMART, INC.:

Mr. Edward M. Carter
Attorney at Law
Jones Day
325 John H. McConnell Boulevard
Suite 600
Columbus, Ohio
(614) 281-3838
emcarter@jonesday.com

FOR DEFENDANTS CVS PHARMACY, INC.; CVS INDIANA, LLC; CVS RX SERVICES, INC.; CVS TN DISTRIBUTION, LLC and OHIO CVS STORES, LLC:

Messrs. Steven N. Herman and Jason B. Acton
Attorneys at Law
Zuckerman Spaeder
1800 M Street Northwest
Suite 1000
Washington, DC 20036-5807
(202) 778-1800
sherman@zuckerman.com
jacton@zuckerman.com

A P P E A R A N C E S (Continuing)

(All Appearing Remotely)

FOR THE DEFENDANTS GIANT EAGLE, INC. and HBC SERVICE COMPANY:

Ms. Erin Gibson Allen
Attorney at Law
Marcus & Shapira LLP
One Oxford Centre
35th Floor
Pittsburgh, Pennsylvania 15219
(412) 471-3490
allen@marcus-shapira.com

OTHERS PRESENT:

Mr. David R. Cohen
Special Master
David R. Cohen Co. LPA
24400 Chagrin Boulevard, Suite 300
Cleveland, Ohio 44122
(216) 831-0001
david@specialmaster.law

Mr. Stephen Kent, Videographer
Veritext Legal Solutions

INDEX OF EXAMINATION

INDEX OF EXHIBITS

INDEX OF EXHIBITS (Continuing)

INDEX OF EXHIBITS (Continuing)

INDEX OF EXHIBITS (Continuing)

INDEX OF EXHIBITS (Continuing)

S T I P U L A T I O N

IT IS STIPULATED AND AGREED, by and between the parties, through their respective counsel, that the deposition of KATHERINE KEYES, PH.D. may be taken before Laura H. Nichols, Commissioner, Certified Realtime Reporter, Registered Professional Reporter and Notary Public;

That it shall not be necessary for any objections to be made by counsel to any questions, except as to form or leading questions, and that counsel for the parties may make objections and assign grounds at the time of trial, or at the time said deposition is offered in evidence, or prior thereto.

I, Laura H. Nichols, a Certified Realtime Reporter and Registered Professional Reporter of Birmingham, Alabama, and a Notary Public for the State of Alabama at Large, acting as Commissioner, certify that on this date, as provided by the Federal Rules of Civil Procedure of the United States District Court, and the foregoing stipulation of counsel, there came before me remotely via Zoom, on June 3, 2021, commencing at 11:09 a.m. EDT, KATHERINE KEYES, PH.D., witness in the above cause, for oral examination, whereupon the following proceedings were had:

* * *

THE VIDEOGRAPHER: Good morning. We are going on the record at 11:09 a.m., EST, on June 3rd, 2021.

When you are not speaking, please mute your audio input as your microphone is sensitive and can pick up whispering and background noise. Please turn off all cell phones or place them away from your computer as they can interfere with the deposition audio. Audio and video recording will continue to take place unless all parties agree to go off the record.

This is Media Unit 1 of the video-recorded deposition of Dr. Katherine Keyes, taken by counsel for defendant in the matter of In Re: National Prescription Opiate Litigation Track 3 Cases, filed in the United States District Court for the Northern District of Ohio, Eastern Division. Case Number 17-MD-804.

This deposition is being held via videoconference with the witness located in New York. My name is Stephen Kent from the firm Veritext Legal Solutions, and I am the videographer. The court reporter is Laura Nichols, also from Veritext Legal Solutions.

I am not authorized to administer an oath. I am not related to any party in this action, nor am I financially interested in the outcome. All appearances will be noted on the stenographic record.

Will the court reporter please swear in the witness.

KATHERINE KEYES, PH.D.,
having been first duly sworn, was examined and testified as follows:

EXAMINATION BY MR. HERMAN:

Q. Dr. Keyes, we have met before. I am Steve Herman. I represent CVS. It is nice to see you again.

Before we went on the record, we talked a little bit. You received two boxes of exhibits from us, correct?

A. Correct.

Q. And the one that has a sealed envelope is -- my understanding, is right next to you; is that correct?

A. Yes.

Q. Okay. Great. And have those envelopes remained sealed?

A. Yes.

Q. Okay. Thank you. And you understand that CVS is a chain pharmacy, correct?

A. Yes.

Q. And do you understand that Walmart, Walgreens, Rite Aid and Giant Eagle are also chain pharmacies?

A. Yes.

Q. If I refer to a group, the chain pharmacies today, will you understand that to mean that I am referring to CVS, Walmart, Walgreens,

Rite Aid and Giant Eagle?

A. Yes.

Q. Thank you very much. The way we have met before is at a prior deposition. You have testified before, correct, under oath?

A. That's correct.

Q. And would you state your full name for the record? Just --

A. Katherine Keyes.

Q. And you understand that you are under oath today, Professor Keyes?

A. I do.

Q. And if you don't understand one of my questions, please just let me know and I will do my best to ask it in a way that you can understand it, okay?

A. Yes.

Q. And if I ask a question and you give an answer, I will take that as an indication that you understood my question; is that fair?

A. That is fair.

Q. Any reason you can think of that you won't be able to answer my questions fully and accurately today?

A. No.

Q. If you need to take a break at any time, please just let me know and we can take a break as long as there's not a question pending, okay?

A. Yes.

Q. Did you do anything to prepare for your deposition today?

A. I had meetings with plaintiffs' counsel.

Q. About how many meetings did you have with plaintiffs' counsel?

A. Two.

Q. And how long did those meetings last?

A. Approximately two hours each.

Q. Have you done the work that you feel you need to do in order to testify here today?

A. I believe so.

Q. Have you done the work you need to do in order to be able to testify before the jury at trial?

A. I believe so.

Q. Is there any data that you wanted that you did not have in writing your report?

A. No.

(Exhibit 1 was marked for

identification.)

Q. (BY MR. HERMAN:) Let's go ahead and mark Exhibit 1, which will be a copy of your report, dated April 16th, 2021.

Exhibit 2, which is the exhibits to your report. And those should be in the sealed envelopes marked CVS 1 and CVS 2.

(Exhibit 2 was marked for identification.)

Q. (BY MR. HERMAN:) If you want to go ahead.

A. Go ahead --

Q. Yeah, thank you.

(Exhibit 3 was marked for identification.)

MR. HERMAN: And we are also going to mark as Exhibit 3 -- and I am not sure -- it won't be there in paper copy, but it is a supplemental materials considered list that was sent to us last night.

Q. (BY MR. HERMAN:) Dr. Keyes, have you opened --

A. I am opening Exhibit 2.

Q. Just let me know when you have them. It is not as easy as when I can hand it across the

table.

A. The tape is really tight.

Q. I did not tape it, but I apologize.

A. I have the exhibit.

Q. Okay. And is Exhibit 1 a copy of your expert report that you submitted on April 16th, 2021?

A. Yes.

Q. And that is a report you wrote for this case?

A. Yes.

Q. Do you understand that when you wrote the report, dated it and signed it that it was to include all the opinions that you intend to offer at trial?

A. Yes.

Q. Does your report contain all the opinions you intend to offer in this case?

A. Yes.

Q. Do you have any corrections to make to your report at this time?

A. I don't at this time.

Q. In your report, you cite with end notes a number of materials. And my understanding is those citations are to the materials that

support the statements and opinions in your report; is that correct?

A. Yes.

Q. And those cited references are on Pages 62 to 76 of your report?

A. Yes, the full references from the footnotes are on Page 62 to 76.

Q. Okay. And besides the materials that you cited as footnotes and your background and experience, are you relying on anything else to support the opinions in your report?

A. In addition to the materials considered list.

Q. Okay. When we were last together, I guess, your materials considered list is, I believe, seventeen hundred items long.

When we were last together, I think you told me that those were materials that you had reviewed, but the ones that were germane to your opinions are the ones that you cited in the end notes to your report. Is that still the case?

A. I would say that the citations that are listed in the report form the basis of many of my opinions, although I also considered the additional sources that are on the materials

considered list as well.

So I would -- I would say both were important in informing my opinions.

Q. And I mean you recognize that your materials to consider list contains -- and that is Exhibit -- well, let's go and do this this way: So Exhibit 2 is your exhibits to your report in this case, correct?

A. Yes, it is my CV --

Q. That is Exhibit A?

A. And Exhibit B is the materials considered list, yes.

Q. And the materials considered list contains, I believe, seven -- one thousand seven hundred and seventy-eight numbered items?

A. Yes, it does.

Q. And on that list it appeared to me that there were materials that you had considered not just in connection with this case but materials that you considered in connection, for example, with the Cabell County, West Virginia case, correct?

A. Yes. And other counties as well.

Q. Okay. And so, for example, Number 86 is related to hospital standard charges in Cabell

County, West Virginia, right?

A. Number 86, Cabell-Huntington Hospital standard charges.

Q. And does that relate to your opinions in this case? That relates to -- well, this case is -- let me ask you this: You understand this case relates to Lake and Trumbull County, Ohio?

A. I do.

Q. So does that material considered Number 86 relate in any way to the opinions you are giving in this case?

A. I would say that, you know, as I have developed expertise across these counties, really considering and comparing, it helps me to form a general opinion about, you know, the extent and burden of opiate use disorder and other related overdose problems across counties.

So I didn't use Cabell data to inform my estimates about Lake and Trumbull but generally considering material from across counties is actually very helpful in developing my opinions more generally.

Q. And I think the last time we were together, when I asked you about some of the depositions, and there are a number of depositions

listed on your chart, you said you had looked at some of them to some degree, but you hadn't read them in full -- all of them in full. Is that still the case today?

MR. ARBITBLIT: Objection, vague.

A. Yeah, I have looked at a number of depositions. And the extent to which I reviewed them depends on the specific deposition and how I was using it to inform my opinions.

Q. (BY MR. HERMAN:) Okay. All right. Well, you do recognize that the materials listed on your materials considered list is probably thousands of pages of material?

A. Yes.

Q. And is it your testimony that you reviewed all that material carefully?

A. It really depends on the specific material. Some material requires a more careful review than other material. Some material I could review and know rather quickly the extent to which it was helpful in forming my opinion. So it really depended on the source.

Q. But as a general matter, if I want to understand what you are relying on to support the statements in your report, I should look at the

materials that you cited as end notes in the report, correct?

MR. ARBITBLIT: Objection, vague.

A. I would say both the end notes and the materials considered list would be potential sources that informed my opinions.

Q. (BY MR. HERMAN:) Okay. Exhibit D is a list of the cases where you -- Exhibit D to Exhibit 2 of this deposition is a list of the cases where you provided testimony. Is that correct?

A. Is that in a separate -- I only have through Exhibit C as part of Exhibit 2.

Q. Okay. Well, let me just try it this way, then. I don't know why that last two pages is not attached to yours, but -- you testified in a case involving Cuyahoga and Summit County, correct?

A. Correct.

Q. Okay. And you testified there under oath?

A. Yes.

Q. And did you have an opportunity to review that transcript after your deposition?

A. I did.

Q. And you also testified in a case that involved Suffolk County, Nassau County and the

State of New York?

A. Yes.

Q. And you gave a deposition in that case?

A. I did.

Q. And you also testified at a hearing before Judge Garguilo?

A. I did.

Q. And your testimony in that case, both at your deposition and at the hearing, were under oath?

A. Yes.

Q. Did you review your transcripts?

A. Yes.

Q. And you have also testified at a case involving Cabell County and the City of Huntington, West Virginia; is that correct?

A. Yes.

Q. And in that case you gave two depositions?

A. Yes.

Q. And both of those depositions were under oath?

A. Yes.

Q. And did you have a chance to review

your transcript for both those depositions?
A. Yes.
Q. Going back to your report in this case, your report in this case doesn't mention CVS, Rite Aid, Walgreens, Walmart or Giant Eagle, correct?
A. That's correct.
Q. You didn't consider any document produced by CVS in this case or any other, correct?
A. As far as I know, no document produced by the -- the defendants.
Q. Okay. And when you say "the defendants," you are including in that CVS, Walgreens, Walmart, Rite Aid and Giant Eagle?
A. Yes.
Q. You didn't review any -- the deposition of any CVS employee, correct?
A. That's correct.
Q. You didn't review the deposition of any Walgreens, Walmart, Rite Aid or Giant Eagle employee, correct?
A. That's correct.
Q. I searched your report for the words "CVS," "Rite Aid," "Walgreens," "Walmart" and "Giant Eagle," and they don't appear anywhere in

your report, correct?

A. I include various data sources that provide aggregate information on retail pharmacies across the United States.

Q. Any pharmacy, correct, any retail pharmacy?

A. On a wide variety of pharmacies.

Q. That is true, the word "pharmacy" does appear six times in your report. Does that sound about right?

MR. ARBITBLIT: Objection, vague.

A. I have not done -- right. I have not done a check on the word "pharmacy," but there is considerable information about pharmacies in the report.

Q. (BY MR. HERMAN:) But you don't specifically mention CVS, Rite Aid, Walgreens, Walmart or Giant Eagle in your report, correct?

A. That is correct.

Q. You don't intend to offer any opinions specific to CVS, correct?

A. To the extent that I offer opinions about pharmacies, I would include CVS as one of them. But I don't have any specific opinions about CVS uniquely.

Q. Well, I think we are saying the same thing. You are not going to offer opinions specific to CVS in this case, correct?

MR. ARBITBLIT: Objection. Asked and answered.

A. I offer opinions about the pharmacies overall. There is nothing that is specific to any particular pharmacy chain.

Q. (BY MR. HERMAN:) And just so the record is clear, when you say "specific to any pharmacy chain," you are including in that Walgreens, Walmart, Rite Aid and Giant Eagle?

A. That's correct.

Q. Professor Keyes, this may be a somewhat silly question, but have you ever worked in a pharmacy?

A. I have never worked in a pharmacy.

Q. You don't hold yourself out as an expert in the practice of pharmacy?

A. I have expertise in the epidemiology of pharmacological distribution and harms associated with medications that are dispensed from pharmacies.

Q. Okay. But you yourself have never practiced pharmacy?

A. I am not a pharmacist.
Q. And are you an expert in the laws and regulations that apply to pharmacies?
A. I have expertise and knowledge based on my epidemiological background on laws and regulations as they apply to pharmacies.
Q. So do you hold yourself out as an expert in the Controlled Substances Act?
A. I hold myself out as an expert in policies and laws as they relate to pharmacies, which would include the Controlled Substances Act.
Q. And -- okay. You are not evaluating whether any specific prescription was written by a prescriber for a legitimate medical purpose in this case, are you?
A. No. Oh, yes. I'm sorry. I was -- I am not providing any opinions about specific prescriptions, right.
Q. So just so the record is clear, because I think -- okay. I think that is clear.
Are you aware of any prescription opioid improperly dispensed by a CVS pharmacy in Lake or Trumbull County?
A. I have not evaluated information related to specific prescription opioids dispensed

in Lake or Trumbull County.

Q. Okay. And you didn't look at what happened to any specific patient who filled a prescription at any pharmacy in Lake or Trumbull County, correct?

A. That is correct.

Q. You are not opining that a specific prescription dispensed in Lake County led to harm?

A. I have not evaluated specific prescription information, so I am not opining that -- about any specific prescription in a singular. I am opining about the aggregate.

Q. And you are not opining about any specific patient who filled a prescription either, correct?

A. That is correct.

Q. Okay. Prescription opioids are medications approved for medical use by the United States Food and Drug Administration, correct?

A. Yes.

Q. And to this day, prescription opioids are approved by the FDA for medical use in the United States, correct?

A. Yes.

Q. Have you heard of the Center For Drug

Evaluation and Research?

A. Yes.

Q. And is that part of the FDA?

A. Yes.

Q. Can I ask you to go ahead and open up CVS 3? And I think we will mark that as Exhibit 4.

(Exhibit 4 was marked for identification.)

Q. (BY MR. HERMAN:) Do you have that open now?

A. I do.

Q. Okay. And Exhibit 4 is a printout from the FDA's website on the Development and Approval Process. Do you see that?

A. I see the document that has been given to me. I haven't verified.

Q. But if you look down at the bottom of the page, do you see a website that says https://www.fda.gov/drugs/development-approval-process-drugs? Do you see that?

A. I do, yeah.

Q. Does that indicate to you that this was printed out off the FDA's government website?

A. Yes.

Q. And if you look at the top, second

paragraph in, it says, "The center's best-known job is to evaluate new drugs before they can be sold. CDER's evaluation not only prevents quackery but also provides doctors and patients information they need to use medicines wisely. The center ensures that drugs, both brand name and generic, work correctly and that their health benefits outweigh their known risks." Did I read that correctly?

A. That is what is written.

Q. And do you understand that CDER to be an abbreviation for the Center -- I'm sorry, for the Center for Drug Evaluation and Research?

A. Yes.

Q. Okay. And so the FDA says on its website that one of its roles is to provide doctors and patients information needed to use medicines wisely?

A. That is what the FDA says on their website.

Q. And the FDA says that CDER ensures that drugs work correctly and that their health benefits outweigh their known risks?

MR. ARBITBLIT: Objection. The document speaks for itself. There's no point just reading the document with the witness.

Q. (BY MR. HERMAN:) You can answer my question.

A. I see that written on this page.

Q. On the FDA's website?

A. Yes.

Q. Okay. And if you go down under the heading "FDA Approval: What it Means," it says, "FDA approval of a drug means that data on the drugs' effect have been reviewed by CDER and the drug is determined to provide benefits that outweigh its known and potential risks for the intended population."

MR. ARBITBLIT: Same objection.

Q. (BY MR. HERMAN:) Did I read that correctly?

A. Yes, it was read correctly.

Q. So the FDA states on its website that its approval of a prescription opioid medication means that it has determined that the benefit of prescription opioids outweigh the potential risks for the treatment of moderate to severe pain?

MR. ARBITBLIT: Same objection.

A. That is not what is written here.

Q. (BY MR. HERMAN:) Well, I apologize. Why don't we go to Page 5 of your report. And just

directing your attention to the definition of prescription opioids. In your report you define prescription opioids as "Drugs approved for medical use in the United States for control of moderate to severe pain that are either natural opiate analgesics derived from opium (morphine and codeine), semisynthetic opioid analgesics (oxycodone, hydrocodone, hydromorphone and oxymorphone), synthetic opioids (methadone) or synthetic opioid analgesics (e.g., tramadol and fentanyl)." Is that how you define prescription opioids?

A. Yes.

Q. So your definition of prescription opioids recognizes that they have been approved by the FDA for medical use in the United States for the control of moderate to severe pain, correct?

A. Yes.

Q. And I said "they" there. Just to be clear, I was referring to prescription opioids; you understood that, right?

A. Yes.

Q. And so if you would -- if you take your definition and what the FDA says approval means, would you agree with me that the FDA

approval means that prescription opioid medications -- that the FDA has determined that the benefits of prescription opioids outweigh their potential risk for the treatment of moderate to severe pain?

A. I have not evaluated the specific FDA determination on specific opioid products. I do agree that the FDA has approved prescription opioids and that what is written on this page describes very generally the approval process in a very high level way. But I wouldn't concede that -- without having reviewed the FDA's actual material on opioids, I would not offer an opinion about the FDA's approval process of opioids.

Q. But your definition at least recognizes that they have been approved for treatment of moderate to severe pain, correct?

A. Yes.

Q. And the FDA states on its website that its "evaluation of each prescription opioid medication provides the doctors and patients with information needed to use the medication wisely."

MR. ARBITBLIT: Objection. The document speaks for itself.

A. Yes, that is stated on the website.

Q. (BY MR. HERMAN:) Okay. And can I ask you to go to the next page, 2 of 4, to the section "Strategies for Managing Risks." And the first sentence -- the first and second sentence there say, "All drugs have risks. Risk management strategies include an FDA-approved drug label which clearly describes the drug's benefits and risks and how the risk can be detected and managed." Did I read that correctly?

MR. ARBITBLIT: The document speaks for itself.

A. Yes, it was read correctly.

Q. (BY MR. HERMAN:) Are you aware that the FDA approved a warning label for each prescription opioid medication?

A. I have not evaluated and don't offer opinions on specific FDA warning labels for opioid medications.

Q. Well, I am asking, I think, a slightly different question. You do have an understanding that each prescription opioid medication has a warning label approved by the FDA?

A. Yes.

Q. Is it your understanding that the expectation is that prescribers will review the

warning labels and utilize the information when deciding whether to prescribe prescription opioids?

MR. ARBITBLIT: Objection, vague. Speculative.

A. Yes. I am not offering an opinion about what prescribers review vis-à-vis warning labels.

Q. (BY MR. HERMAN:) Well, is it your understanding that one of the purposes of the FDA warning label for any medication is that prescribers will review that warning label to better understand the risks and benefits of the medication?

MR. ARBITBLIT: Objection, vague. Overbroad.

A. I have not evaluated documents regarding the purpose of the FDA warning label, so I would not offer an opinion on that.

Q. (BY MR. HERMAN:) Okay. You don't have any understanding of the purpose of an FDA warning label?

MR. ARBITBLIT: Objection. Argumentative.

A. I have not evaluated any specific material on the purpose of FDA warning labels, so I

would not -- I would not offer an opinion about what prescribers do vis-à-vis specific warning labels regarding opioids.

Q. (BY MR. HERMAN:) What is your understanding of the purpose of an FDA-approved warning label?

A. I believe that it is -- you know, the document here states very clearly that the purpose of the warning label is to provide information about potential risks and side effects.

Q. Okay. And like its name suggests, it is intended to be a warning that doctors will review before prescribing medication, right?

MR. ARBITBLIT: Objection, speculative.

A. I think there are numerous reasons to have a warning label, and I would not offer an opinion about the -- what specific doctors and prescribers do with those warning labels.

Q. (BY MR. HERMAN:) Do you agree that approval by the FDA of prescription opioid medications was a necessary condition for there to be a supply of prescription opioids?

A. Not in an absolute sense.

Q. Well, without approval of

prescription opioids by the FDA, no doctor would prescribe opioids to patients, correct?

A. That is correct.

Q. And CVS, Rite Aid, Walmart, Walgreen's and Giant Eagle's pharmacies would not have prescription opioids in their pharmacies if they were not approved by the FDA as medications, correct?

A. That's correct.

Q. Professor Keyes, do you fault the FDA for approving prescription opioids for medical use?

A. I think, in general, when you look at the drivers of the opioid crisis and the overdose crisis, that certainly the role of the FDA in evaluating the risks and benefits of opioid medications is part of the larger constellation of factors that contributed to the opioid crisis.

Q. And so am I understanding you correctly that with information you have today, you do not believe that the FDA evaluated the risks and benefits of the opioid medications appropriately?

A. That is a very general statement. I would -- I would certainly -- I think that one could reevaluate the information that the FDA received, but I would need to look at each specific

drug in determining the appropriateness of FDA conclusions.

Q. And you would have to look at each different drug because there are different types of prescription opioids, correct?

MR. ARBITBLIT: Objection, vague, overbroad.

A. There are different types of prescription opioids.

Q. (BY MR. HERMAN:) And different types of prescription opioid medications have different risks and benefits?

MR. ARBITBLIT: Objection. Vague and overbroad.

A. There are different types of opioid medications -- each one would need to be evaluated in terms of their risks and benefits separately.

Q. (BY MR. HERMAN:) If you were in charge of the FDA, would you have approved prescription opioids for medical use?

MR. ARBITBLIT: Objection, vague, speculative, overly broad.

A. That is a hypothetical that I can't answer. I am not in charge of the FDA, so I can't answer what I would have done had I been in charge

of the FDA.

Q. (BY MR. HERMAN:) I am asking you to answer that hypothetical.

MR. ARBITBLIT: Incomplete hypothetical. Same objection plus incomplete hypothetical.

Q. (BY MR. HERMAN:) Dr. Keyes, if you were in charge of the FDA, would you have approved prescription opioids for medical use?

MR. ARBITBLIT: Same objection.

A. I would need to look at each -- I would need to review the documents for each specific product to answer that question, which I have not done.

Q. (BY MR. HERMAN:) Okay. Sitting here today, you don't know whether you would have approved or banned prescription opioids for medical use?

MR. ARBITBLIT: Objection, vague, overbroad, hypothetical.

A. I would need to review the specific documents in order to engage in that hypothetical, which I have not done.

Q. (BY MR. HERMAN:) So is the answer to my question no, that sitting here today you cannot

state whether you would ban or approve prescription opioids if you were in charge of the FDA today?

MR. ARBITBLIT: Same objection and asked and answered.

A. I would say that the broad hypothetical of all prescription opioids and the inconclusive language of ban or approve is not something that anyone, including, you know, people in charge of the FDA, could answer in an absolute way.

Q. (BY MR. HERMAN:) It is a complicated question?

MR. ARBITBLIT: Object to the form.

A. I don't think it is a complicated question. I think it is a hypothetical that is too broad.

Q. (BY MR. HERMAN:) Can I ask you to take out what has been marked as Exhibit 7-1 in the envelope, and it will be Exhibit 5 to this deposition.

(Exhibit 5 was marked for identification.)

Q. (BY MR. HERMAN:) Do you have that or do you have that exhibit?

A. I do.

Q. And is Exhibit 5 the CDC guidelines that were issued in 2016?

A. They are a set of guidelines that were published in 2016 by the CDC.

Q. And they are a set of guidelines on prescribing opioid medications that were published in 2016?

A. They are recommendations for primary care clinicians who are prescribing opiates for chronic pain outside of active cancer treatment, palliative care and end of life care. So just to be more specific, that is the scope of the guidelines.

Q. Okay. And you cite these in your expert report as it is referenced, 152?

A. Let me just check.

(Pause.)

A. Yes.

Q. (BY MR. HERMAN:) And were the 2016 guidelines the first guidelines put out by the CDC on prescribing opioid medications?

A. I'm not sure. I would need to look at that.

Q. Do you know if the 2016 CDC guidelines were the first federal guidelines on

prescribing opioids?

A. I don't know.

Q. Dr. Keyes, I think in your report you recognize that prescribing of opioids has been decreasing for approximately ten years. Is that correct? Since 2012?

A. Is there a place in the report that I can --

Q. Well, let me ask in the abstract. Do you know when the prescribing -- when generally the prescribing of opioids began to decrease in the United States?

A. I would want to look at my report to make sure I am testifying correctly. Is there a place in the report that I can -- I just want to make sure I am giving the most accurate information.

Q. We can come back to that. You don't know off the top of your head?

A. I just want to make sure because this is important that I am accurately citing the right reference and conveying the right information for the record. And so I would prefer, and be more comfortable, if you could point to where in the report that is stated so I can appropriately

testify.

Q. Okay. So if you look at Page 45, at the top, and there's a sentence there that recognizes that prescribing began to decrease in 2012. Do you see that sentence?

A. The sentence is "Prescribing then began decreasing, although remains extraordinarily high."

Q. Okay. But you recognize that prescribing began to decrease in 2012, correct?

A. Right. From the height of 2012.

Q. And has prescribing of prescription opioids continued to decrease since 2012?

A. Nationally or in Lake and Trumbull County?

Q. Well, let's start with nationally.

A. Nationally, prescription opioid use has declined, although it remains much higher than preopioid epidemic levels. So, yes, there have been declines since 2012, but the level of prescribing remains much higher than it was prior to the opioid crisis.

Q. And when higher -- when you say "higher than," can you give me a year when you are comparing it to?

A. The sources that I cite in this report began in about the mid 1990s.

Q. Do you know if opioid prescribing had begun to increase before the mid 1990s?

A. In the sources that I have evaluated, most of the -- the sources that I have evaluated began in the early to mid 1990s. So I am not -- I have not evaluated carefully sources prior to the early to mid 1990s.

Q. Okay. And can I ask you -- I think I know the answer to this based on your past testimony. But if you look at Exhibit 5, first sentence of Background, it says opioids are commonly prescribed for pain. Do you agree that opioids are a commonly prescribed medication for pain?

A. I agree that opioids are commonly prescribed for pain.

Q. And you have been talking a little bit about the rate of prescribing. Do you understand that to mean that licensed prescribers often prescribe opioids for their patients' pain?

MR. ARBITBLIT: Objection. Speculative.

A. I understand that -- that opioids are

prescribed often for pain by licensed prescribers, yes.

Q. (BY MR. HERMAN:) And can I direct your attention to the second paragraph of Exhibit 5.

MR. HERMAN: Is there any way we can put that up?

Q. (BY MR. HERMAN:) Do you see where it says, "Prevention, assessment and treatment of chronic pain are challenges for health providers and systems. Pain might go unrecognized and patients, particularly members of racial and ethnic minority groups, women, the elderly, persons with cognitive impairment and those with cancer and at the end of life, can be at risk for inadequate pain treatment." Do you see where I am reading?

A. I do.

Q. Did I read that correctly?

A. Yes.

MR. ARBITBLIT: Objection. The document speaks for itself.

Q. (BY MR. HERMAN:) And is it your understanding that the CDC is expressing a concern that pain might go unrecognized and untreated in 2016?

MR. ARBITBLIT: Objection. The document speaks for itself, and it is speculative as to what the CDC is thinking.

A. I can read what is on the page. This document, coauthored by three people through the CDC, states that there can be persons who are at risk for inadequate pain treatment.

Q. (BY MR. HERMAN:) I found it interesting that pain going unrecognized was a particular concern to women. Do you know why that would be the case, Professor Keyes?

MR. ARBITBLIT: Object to the form.

A. I guess I don't understand the question. Is the question, is it interesting that pain goes unrecognized?

Q. (BY MR. HERMAN:) Oh, no, I'm sorry. Let's get rid of my discussion of that point.

I just want to know, do you know why it would be the case that pain would be of particular concern for going unrecognized for women?

A. I'm not sure what specifically the CDC authors are referring to when they highlight women as a risk group there.

Q. Would your answer be the same for

ethnic and racial minority groups?

A. I believe what the purpose of the sentence is is that the sentence is saying pain may go unrecognized and that that might be different by these different demographic groups, and that would include racial and ethnic minorities and women and the other groups highlighted in that sentence.

Q. Yeah, I understood it to be saying that these groups can be particularly at risk for inadequate pain treatment. Is that how you understand it or --

MR. ARBITBLIT: Object to the form.

A. That is not exactly what the sentence says. It says that those groups can be at risk for inadequate pain treatment, based on the CDC -- these authors' assessment.

Q. (BY MR. HERMAN:) Okay. And these authors' assessment published by the CDC?

A. Yes.

MR. ARBITBLIT: Object to the form.

Q. (BY MR. HERMAN:) And if you look at the next sentence, it says, "Patients can experience persistent pain that is not well-controlled. There are clinical, psychological and social consequences associated with chronic

pain, including limitations in complex activities, lost work productivity, reduced quality of life and stigma, emphasizing the importance of appropriate and compassionate patient care."

Do you see where I just read?

A. I do.

Q. Did I read that correctly?

A. Yes.

Q. Do you agree with the CDC that there are clinical, psychological and social consequences associated with chronic pain?

A. There certainly can be consequences of chronic pain, including clinical, psychological and social.

Q. And do you understand the CDC to be saying here because of clinical -- sorry -- sociological and social consequences associated with chronic pain, that emphasis should be placed on the importance of appropriate and compassionate care?

A. I think -- do -- you are asking what I understand the CDC to be saying? I don't want to speculate about what the CDC meant in that statement. I am not the authors.

Q. Would you agree with the sentiment

that because there are clinical, psychological and social consequences associated with chronic pain, that emphasis should be placed on the importance of appropriate and compassionate patient care?

A. All patients, regardless of their condition, should be treated with appropriate and compassionate care. And there's a lot of discussion about the level -- what constitutes appropriate care in the context of chronic pain.

Q. And I think the -- and can I ask you to go to Page 2? And if you look just above "Rationale," do you see where it says, "Clinical decision-making should be based on a relationship between the clinician and patient and understanding of the patient's clinical situation, functioning and life context. The recommendations in the" -- well, let's stop.

"The recommendations in the guideline are voluntary rather than prescriptive standards. They are based on emerging evidence, including observational studies or randomized clinical trials with notable limitations. Clinicians should consider the circumstances and unique needs of each patient when providing care."

MR. ARBITBLIT: Objection. The

document speaks for itself. No question pending.

Q. (BY MR. HERMAN:) Do you see where I just read?

MR. ARBITBLIT: Same objection.

A. I see that that is what is written.

Q. (BY MR. HERMAN:) And did I read that correctly?

A. You read that correctly.

Q. Clinical decisions are decisions made by prescribers, correct?

MR. ARBITBLIT: Objection.

A. Clinical decisions can be made by prescribers.

Q. (BY MR. HERMAN:) Do you agree that the clinical decisions being referenced here are clinical decisions made by prescribers?

MR. ARBITBLIT: Objection, speculative. The document speaks for itself.

A. I wouldn't speculate on specifically who the CDC was referring to in that sentence. They just say "clinical decision-making." Clinical decisions are made by a variety of care providers.

Q. (BY MR. HERMAN:) Well, these are prescribing guidelines, are they not?

A. These are prescribing guidelines.

Q. And so you don't think that the reference to clinical decisions is a reference to the prescriber, decisions made by prescribers?

MR. ARBITBLIT: Objection, speculative. Asked and answered. Argumentative.

A. I am not speculating on who -- they -- I am reading the text, as you are. They discuss the dose response relationship between opioid use and overdose and then say that clinical decision-making should be based on a relationship between a clinician and a patient. They do not specify provider.

Q. (BY MR. HERMAN:) Okay. Right in the next sentence it says -- let me ask you this: Dr. Keyes, you understand that a doctor is only supposed to write a prescription for a legitimate medical purpose, correct?

MR. ARBITBLIT: Object to form. Speculative.

A. I don't want to speculate about what every doctor writes prescriptions for.

Q. (BY MR. HERMAN:) Well, I am not asking you about why the doctor does it. But I am asking you -- well, let me ask you this: You said earlier that you had familiar -- familiarity and

expertise with the CSA and related laws and regulations, correct?

A. Yes.

Q. Okay. So do you understand that a doctor is only supposed to write a prescription for a legitimate medical purpose?

MR. ARBITBLIT: Object to form.

A. I would ask what you mean by a legitimate medical purpose. There's -- doctors write prescriptions based on information that they have.

Q. (BY MR. HERMAN:) You understand that that is the language used in the CDC, that a practitioner is only supposed to write a prescription for a legitimate medical purpose in the usual course of practice?

A. Is this a specific CDC document?

Q. Well, it is a specific law and regulation. I thought earlier you said you had expertise in the CSA and laws and regulations.

MR. ARBITBLIT: Objection.

A. From the CDC?

Q. (BY MR. HERMAN:) No, from the federal government.

MR. ARBITBLIT: Objection.

Misstates.

A. So your previous question was about language used by the CDC. So my question is --

Q. (BY MR. HERMAN:) No. My --

A. -- if there's a specific --

Q. (BY MR. HERMAN:) I'm sorry. I didn't mean to interrupt. My previous question was you understand that a doctor is only supposed to write a prescription for a legitimate medical purpose, correct?

MR. ARBITBLIT: Objection, vague.

A. My understanding is that physicians write prescriptions based on the information that they have about the patient and that -- and that they use that information in writing prescriptions.

Q. (BY MR. HERMAN:) Well, let's see if we can agree. Would you agree that the doctor, based on information the doctor has, is supposed to write a prescription in good faith for a legitimate medical purpose?

A. I think that there is a wide variety of opinions about the medical purposes for which opioids would be an effective therapy. And so two doctors could have differences of opinion about the specific medical purpose for which an opioid would

be indicated. Therefore, my opinion is that physicians write prescriptions based on the information that has been provided to them.

Q. So I understood you to be saying -- you said different physicians might evaluate a prescription differently, correct?

MR. ARBITBLIT: Objection. Misstates the testimony.

Q. (BY MR. HERMAN:) Well, you said two doctors could have differences of opinions about the specific medical purpose for which an opioid would be indicated, correct?

A. I said that two doctors could have differences, yes, about the specific medical purpose for which an opioid would be indicated.

Q. That is because doctors might evaluate the risks and benefits of a prescription opioid differently?

MR. ARBITBLIT: Object to form.

A. That is not what I testified.

Q. (BY MR. HERMAN:) Okay. Well, what do you mean when you say two doctors could have differences of opinions about the specific medical purpose for which an opioid would be indicated?

A. I was referring in that statement to

the statement that doctors write prescriptions for legitimate medical needs. My opinion is that the word "legitimate" is fairly vague.

Q. Okay. So you think the term "legitimate medical purpose" is too vague to evaluate?

MR. ARBITBLIT: Object to form.

A. It is broad.

Q. (BY MR. HERMAN:) Different people could evaluate it differently?

A. I think what we have seen from the evidence, and I would just go back to my report, is that -- is that the opioids that were dispensed often went to the wrong people. And, therefore, because you have this vast oversupply, it certainly is indicative of a wide variety of dispensing and prescribing practices and that legitimate medical needs were not always the -- that opioids were not prescribed always for legitimate medical needs because there was such an oversupply and diversion.

Q. But do you have a reason to believe -- well, let me -- let me ask you this: I mean, do you believe that -- you talked earlier about how doctors were prescribing based on the information available to them. Do you believe that

the doctors who were prescribing based on the information available to them intended that the prescriptions would be used for a legitimate medical purpose?

MR. ARBITBLIT: Objection, vague, overbroad, speculative. Misstates the record.

A. I wouldn't offer an opinion about all doctors and their intentions for prescribing.

Q. (BY MR. HERMAN:) I want to go back to my question, because you have been sort of focusing on the -- understanding the intention of the doctor. But do you understand that a doctor is only supposed to write a prescription for a legitimate medical purpose?

MR. ARBITBLIT: Objection, vague. Object to the prelude.

A. When -- I guess I am not understanding what you mean by a doctor is supposed to write a prescription. I think, as it says in the CDC guidelines, clinicians and patients are in conversation about various conditions. And so what the intention of doctors are, what they are supposed to do and what is actually done in a clinical setting -- you know, I'm not sure what you are asking.

Q. (BY MR. HERMAN:) Well, do you understand that the federal regulations on prescribing controlled substances state that a practitioner should only prescribe controlled substances for a legitimate medical purpose?

A. I do understand the federal regulations on that -- on that issue.

Q. Okay. So you do have an understanding that a doctor is only supposed to prescribe a prescription opioid for a legitimate medical purpose?

MR. ARBITBLIT: Objection, form.

A. My understanding of the federal regulations is that controlled substances should be prescribed for approved uses.

Q. (BY MR. HERMAN:) Okay. Do you understand that it actually uses the term "legitimate medical purpose"?

THE REPORTER: You need to speak up a little bit, Mr. Herman.

MR. HERMAN: I apologize. I leaned back.

Q. (BY MR. HERMAN:) Let me ask my question again. Do you understand that the federal regulation actually uses the term "legitimate

medical purpose"?

A. I would need to review the specific document to understand it in context.

Q. Okay. Going back to the guidelines, when it says that the guidelines are voluntary rather than prescriptive standards, do you understand that to mean they are not absolute rules?

MR. ARBITBLIT: Object to form.

A. I would just refer to the document itself. It says that they are voluntary rather than prescriptive standards. And I wouldn't offer an opinion about how those are interpreted -- how those words are interpreted.

Q. (BY MR. HERMAN:) Okay. All right. Well, do you understand that part of the reason they are guidelines and not prescriptive standards is explained in the next sentence, that "They are based on emerging evidence, including observational studies or randomized clinical trials" --

THE REPORTER: I can't understand you well. Would you slow down when you are reading and speak up?

MR. HERMAN: I apologize.

Q. (BY MR. HERMAN:) Do you understand

the next sentence, "They are based on emerging evidence, including observational studies or randomized clinical trials with notable limitations," to be part of the explanation for why the guidelines are not prescriptive standards?

MR. ARBITBLIT: Objection, speculative.

A. Yeah, I don't -- I can't speak to whether that sentence is being offered as part of the previous sentence.

Q. (BY MR. HERMAN:) Okay. Well, the CDC in that sentence recognizes that evidence related to prescription opioids has changed over time, correct?

A. I'm sorry. You are cutting out a little bit.

SPECIAL MASTER COHEN: Mr. Herman, I'm sorry. This is David Cohen. I just note that your appearance on my screen is actually much smaller than everyone else. And so I wonder if you are a distance from the microphone and that is what is causing the issue.

MR. HERMAN: I am a little bit of a distance, but I haven't moved since the start. Can people hear me now?

SPECIAL MASTER COHEN: Yeah. It has actually been hard to hear from the start. So I am just suggesting that if you get closer to the microphone, it might be helpful.

MR. HERMAN: Okay. Do people want to -- do people want to break for -- maybe just take a break and maybe break for lunch now and I could try to get this straightened out?

THE VIDEOGRAPHER: Sure. Stand by. We are now off the record. The time on the video monitor is 12:14.

(Whereupon, a lunch break was had from 12:14 p.m. until 12:48 p.m. EDT)

THE VIDEOGRAPHER: We are now on the record. The time on the video monitor is 12:48.

MR. HERMAN: Can we go off the record for a second? I really apologize. I lost my realtime because of whatever they changed. And so I didn't realize that until just now. So --

THE VIDEOGRAPHER: Stand by.

MR. HERMAN: I apologize.

THE VIDEOGRAPHER: We are now off the record. The time on the video monitor is 12:49.

(Whereupon, a break was had from 12:49 p.m. until 12:52 p.m. EDT)

THE VIDEOGRAPHER: We are now on the record. The time on the video monitor is 12:52.

(Exhibit 6 was marked for identification.)

Q. (BY MR. HERMAN:) Dr. Keyes, can I ask you to open CVS 5? And Exhibit 5 is an article on which you were an author, titled "A Critical Review of the Social and Behavioral Contributions to the Overdose Epidemic" that was published in -- on November 30th, 2020. Is that correct?

A. Yes.

Q. And can I ask you to turn to Page 97? And under "Supply Drivers of the Overdose Epidemic," this article states, "Supply drivers include the proliferation of opioids prescribing to treat chronic pain, as well as changes in the heroin and the illegally manufactured opioid synthetics market." Is that correct?

A. That's correct.

Q. And so this article says there were two -- the two supply drivers discussed are, one, more prescribing and, two, changes in heroin and illegally manufactured synthetics market?

A. Yes.

Q. And if you go down, the next

paragraph, it says, "The supply side routes of the overdose epidemic in the United States lie at the intersection of two social and behavioral forces that together led to the proliferation of opioid prescribing in the 1990s, especially for noncancer, acute and chronic pain conditions."

Did I read that correctly?

A. You did.

Q. Okay. And so your article is saying there are two forces that combine to lead to an increase in opioid prescribing by physicians, correct?

A. The article does not mention by physicians, just prescribing, including dispensing.

Q. Well, is it your understanding that CVS -- well, any pharmacy is only supposed to dispense a prescription if they receive a -- well, only supposed to dispense a prescription to a patient if they receive a prescription from a -- written by a licensed prescriber?

A. That's correct.

Q. Okay. So the first step is, there has to be a prescription written by a doctor, correct?

A. A first step of what?

Q. In order for there to be a proliferation of prescriptions, doctors had to write more prescriptions, correct?

A. There were more prescriptions written by doctors in the 1990s.

Q. Okay. And the article goes on to say, "The first force was a shift in treatment approaches for chronic noncancer pain, including a campaign by professional societies and the U.S. Joint Commission, the nation's largest accrediting body for healthcare organizations, to consider pain as a fifth vital sign and to improve the quality of care for chronic pain." Did I read that correctly?

A. Yes.

Q. And then it goes on to say, "In 1997, the American Pain Society and the American Academy of Pain Medicine released a consensus statement endorsing the use of opioids to treat chronic noncancer pain, arguing that the risk of addiction from opioids was low. At the time, the risk of addiction associated with opioid use was not well understood." Did I read that correctly?

A. You read that correctly.

Q. And so this article that you authored says that the first force that led to increased

prescribing was that people began to approach treating pain differently than they had previously, correct?

A. Correct.

Q. Okay. The medical standard of care for treating pain changed, correct?

MR. ARBITBLIT: Objection, speculative. Outside the scope.

A. That is not what the article states.

Q. (BY MR. HERMAN:) Well, have you yourself said that it became standard practice to use prescription opioids to treat pain?

A. Yes.

Q. And when you used the term "standard practice," you were talking about standard practice by prescribers to treat pain, correct?

A. Are you referring to a specific section of this article or a different article? I just want to make sure I contextualize it appropriately.

Q. Well, I am referring -- well, why don't we try to answer it without an article. When you used the term that it became "standard practice" to use prescription opioids to treat pain, would you be referring to standard practice

by physicians?

MR. ARBITBLIT: Objection. The witness has the right to look at the context.

A. I would prefer -- just to make sure I am testifying correctly, I just want to give you the right information. So there are various articles I have written about pain medicine. And so if there's a specific article you would like me to discuss, I would prefer to see it.

MR. HERMAN: Can you pull up --

Q. (BY MR. HERMAN:) Professor Keyes, can you open Exhibit 12? And Professor Keyes, Exhibit -- well, for this deposition, it is going to be Exhibit 7, I believe.

(Exhibit 7 was marked for identification.)

Q. (BY MR. HERMAN:) Exhibit 7 is an article that you authored called "Understanding the Rural-Urban Differences in Nonmedical Prescription Opioid Use and Abuse in the United States."

A. Sorry. I don't mean to interrupt you. I accidentally opened up the wrong -- this was 7-12, and I accidentally opened it.

Q. That is okay. Just set that aside for now.

A. Okay. I need to find CVS 12.
Q. Okay. Appreciate that.
A. I apologize.
MS. POLLOCK: Steven, will you be uploading that to Exhibit Share?
MR. HERMAN: It is uploading now.
MS. POLLOCK: Thank you.
THE REPORTER: I don't believe you had an Exhibit 6.
MR. HERMAN: I thought --
THE REPORTER: Let me refresh and make sure.
MR. HERMAN: We may have to get this straightened out, but I thought the last one, what we were talking about, "A Critical Review of the Social and Behavioral Contributions to the Opioid Epidemic," is Exhibit 6.
THE REPORTER: Okay. I see that. It is up on Exhibit Share now. Thank you.
Q. (BY MR. HERMAN:) Professor Keyes, do you have CVS 12, what is going to be marked as Exhibit 7 for this deposition now?
A. I do.
Q. Okay. And that is an article titled "Understanding the Rural-Urban Differences in

Nonmedical Prescription Opioid Use and Abuse in the United States" that you are an author on that was published in February 2014?

A. Yes.

Q. And if I could ask you to turn to Page 2 [sic], under the heading, "Self-Medicating for Pain." And do you see where you wrote, "When used as prescribed under medical supervision, opioid analgesics are effective and used as standard practice in managing acute and chronic pain"? Do you see where I am reading?

A. I do.

Q. Okay. And when you use the term "standard practice in managing acute and chronic pain," were you referring to standard medical practice by physicians?

A. Yes.

Q. Okay. Do you believe the opioid epidemic would have occurred if prescribing opioids for medical care for treating pain did not become standard practice?

MR. ARBITBLIT: Objection. Speculative.

A. I think what I have outlined in my report is that there is a constellation of factors

that contributed to the opioid epidemic, and one of those factors was the vast increase in the supply of opioids, including through physician prescription.

Q. (BY MR. HERMAN:) Well, I am asking you, though, a different question, and I would like you to listen.

Do you -- do you believe that the opioid epidemic would have occurred if prescribing opioids did not become standard practice in managing acute and chronic pain?

MR. ARBITBLIT: Objection. Asked and answered.

A. I do not believe it would have occurred, because it is part of that large constellation of factors that led to oversupply.

Q. (BY MR. HERMAN:) You do not believe that the increase in prescribing as standard practice led to the opioid epidemic?

MR. ARBITBLIT: Objection. Asked and answered. Misstates the testimony.

A. The question was: Do you believe that the opioid epidemic would have occurred if prescribing opioids had not become standard practice? And I believe I answered the question

that I do not believe it would have occurred if opioids did not become standard practice, because it led to this oversupply.

Q. (BY MR. HERMAN:) But do you believe that the prescribing of opioids for the treatment of pain as standard practice led to the oversupply of prescription opioids?

MR. ARBITBLIT: Object to form.

A. It was one of the factors that led to oversupply.

Q. (BY MR. HERMAN:) Okay. And going back to Exhibit 6, CVS 5 for you, the article says, "The second, related force involved the pharmaceutical industry's concerted effort to advocate for long-term use of opioids as a safe, nonaddictive, effective, and humane alternative to treat noncancer pain. These marketing efforts accelerated the shift in treatment approaches for chronic noncancer pain."

Did I read that correctly?

A. Yes.

Q. Okay. And the example you go on to give in the next few sentences is about Purdue, right?

A. Yes.

Q. Purdue is a manufacturer, correct?
A. That's correct.
Q. When you refer to the pharmaceutical industry in this sentence, were you referring to Purdue and other manufacturers?
A. I believe several sentences later I define the pharmaceutical industry as including the production, distribution and prescription of opioids proliferated due to the removal of physician sanctions. So the pharmaceutical industry is broadly conceived.
Q. Okay. What is your basis for saying that the marketing efforts that accelerated the shift in treatment approaches for chronic noncancer pain was caused by entities other than manufacturers?
A. Can you point me to where you are looking?
Q. The second force -- so it's at the top of the paragraph, the second force --
A. Uh-huh.
Q. -- "involved the pharmaceutical industry's concerted efforts to advocate for the long-term use of opioids as safe, nonaddictive, effective, and humane alternative to treat

noncancer pain. These marketing efforts accelerated the shift in treatment approaches for chronic noncancer pain."

A. Yes, that is what it says.

Q. Okay. And -- well -- okay. Well, the only example you give is Purdue, a manufacturer. So I am wondering, what basis do you have to say that other -- any part of the pharmaceutical industry other than manufacturers engaged in marketing efforts that accelerated the shift in treatment approaches for chronic noncancer pain?

MR. ARBITBLIT: Object to form. Misstates.

A. I guess I am still not understanding the question. The --

Q. (BY MR. HERMAN:) Well --

A. I say in here that there were "concerted efforts to advocate for the long-term use of opioids as" -- and that those concerted efforts involved the pharmaceutical industry. Several sentences later, I provide context for that statement, saying that -- that the Intractable Pain Act "removed physician sanctions for the use of opioids" and that "the production, distribution,

prescription, and use of opioids proliferated."

So all entities that would be involved in the production, distribution, prescription and use of opioids would be implicated in that statement.

Q. Okay. Well, your report discusses -- and going back to Exhibit 1, your report discusses how direct marketing to physicians increased prescribing, correct?

MR. ARBITBLIT: Objection. Vague.

A. So that section in the report describes three papers that have used data on payments to physicians and associations with various outcomes.

Q. (BY MR. HERMAN:) Okay. And on Page 14, I think that is where you are talking about, you are discussing how direct marketing to physicians increased prescribing, right, and you cite -- I think you just said three papers for that proposition?

A. I am -- I am on Page 14 of the report, but I think it is actually later in the report, just so it is accurate in the record.

Q. So you talk about it at Page 14 and then again at Page 33?

A. Oh, I see. The marketing -- I state in the -- in the report that the "marketing of opioid drugs led to increased sales of the marketed drugs."

Q. Well, you say on Page 14, "Evidence" -- "The increase in opioid prescribing was driven by a multitude of factors, including direct marketing to physicians using data that underestimated opioid use disorder risks in patients, which I detail in Section B. Evidence shows that pharmaceutical marketing of prescription drugs increases prescribers' likelihood of prescribing the marketed drug in the future," right?

A. That is a general statement about prescription drugs and marketing. The next sentence is about opioids.

Q. Yeah. "That is also true for prescription opioids; as a result, increased marketing of opioids led to increased sales of the marketed drugs," right? And you cite a couple of studies?

A. Correct.

Q. The literature that you cite about marketing discusses marketing activities by

pharmaceutical manufacturers to physicians, correct?

A. Is there a specific study that you are referring to?

Q. I am asking about all of them at the moment. The literature that you cite in your report about marketing activities to physicians discusses marketing activities by manufacturers to physicians, correct?

A. Are the articles in the exhibits, because I would just like to confirm that that is what the articles state?

Q. You don't know off the top of your head whether the articles are discussing marketing activities that pharmaceutical manufacturers engage in?

A. There -- the articles refer to a database called the Sunshine Open Payments database, I believe, and I would like to -- I would feel more comfortable giving correct testimony if I could look at the article and make sure that I am describing what is included in the contents of the Open Payments database accurately.

Q. Okay. Well, why don't we look at -- why don't we try 7 -- did you tell me you already

opened 7-12?

A. I did open 7-12, yes.

MR. HERMAN: Why don't we mark it -- mark that as Exhibit 8.

(Exhibit 8 was marked for identification.)

MR. HERMAN: And --

THE VIDEOGRAPHER: Counsel, your screen sharing is in the video.

MR. HERMAN: When -- I am sorry. The screen sharing is in the video. Can you see me?

THE VIDEOGRAPHER: No, the screen -- the screen being shared is in the video. I was just letting him know, whoever was sharing.

MR. HERMAN: Oh.

Q. (BY MR. HERMAN:) Exhibit 8 is an article titled, "Association of Industry Payments to Physicians with the Prescribing of Brand-name Statins in Massachusetts."

A. Yes, that is correct.

Q. Okay. And do you see on Page 763 -- well, let me ask you this: This is one of the articles you cite in your report, correct?

A. Yes, but I don't think it is on -- I don't cite this on Page 14. I believe I cite this

in the other section that discusses the Hadland article. So if I could just pull up that section to make sure I am -- is that correct? To make sure -- do you know which number --

Q. It -- I believe this is Reference 141, so maybe it is --

A. Yeah.

Q. You cite some of them in both places, but I think this is one cite on Page --

A. This is only -- I just wanted to pull up the correct section. Okay.

Q. Okay. Do you see on Page 763, it says, "Payment by pharmaceutical manufacturers to physicians outside the research context may be problematic, because they can be perceived as conflicts of interest that could interfere with physicians' responsibilities to their patients"?

A. This is on Page 763?

Q. Yep, first paragraph.

A. Oh, I see. Yes. I see that.

Q. You see above it says, "In the United States" -- the paragraph begins, "In the United States, many physicians have financial relationships with pharmaceutical manufacturers."

A. I see that.

Q. Okay. Did I read that correctly?
A. You did.
Q. Is it your understanding that this article about payments to physicians relates to manufacturers?
A. That this particular article about statins? You are asking -- you are asking whether --
Q. Well, I am asking -- this is -- you said you would like to see an article. I am -- I -- well, I am asking you, does this article deal with payment by manufacturers?
A. This article does -- the methods section of this paper says that they used two data sources. This -- the data source that was used on payments was the Massachusetts physician Open Payments database, which is derived from pharmaceutical manufacturer reports. But the article does not include opioids, as far as I can tell.
Q. Okay. I -- well, we are short on time. I'm not sure I am going to be able to go through every article.
But sitting here today, do you believe that the literature you cite in your report

about marketing to physicians discusses marketing activities by pharmaceutical manufacturers?

MR. ARBITBLIT: Object to form.

A. I cite a variety of studies. If there's a specific study that you are asking about, I can look at the study and see what was included.

Q. (BY MR. HERMAN:) All right. Let's look at 72-26. Oh, I'm sorry. This is 7-2. we will mark that as Exhibit 9.

(Exhibit 9 was marked for identification.)

A. So it is 7-26?

Q. (BY MR. HERMAN:) Well, 7-2, I'm sorry, and it is Reference 26 in your --

A. Okay. 7- --

Q. -- report. And this is an article entitled, "Association of Pharmaceutical Industry Marketing of Opioid Products to Physicians With Subsequent Opioid Prescribing." Is that correct?

A. That is correct.

Q. And this is one of the papers you cite in your report at both Page 14 and Page 33?

A. Yes.

Q. Okay. And this looked at the Open Payments database that you were asking about?

A. Yes.

Q. And the authors obtained information from the Open Payments database on all transfer of value from pharmaceutical companies to physicians during 2014, right?

A. That's correct.

Q. Okay. And if you would look at Page 862, the "Results" column, do you see where it says, "The three companies with the highest payment totals were INSYS Therapeutics (which manufactures Subsys, the fentanyl sublingual spray), Teva Pharmaceuticals USA, and Janssen Pharmaceuticals"?

A. I see that.

Q. Okay. And do you understand that INSYS, Teva and Janssen are all manufacturers?

A. I do understand that.

Q. And if you turn to Page 863, do you see the first full paragraph, where it says, "Our findings add to prior studies of industry marketing to physicians by examining" -- oh, sorry. Strike that.

Do you see the last paragraph? After the introductory clause, it says, "our findings suggest that manufacturers should consider a voluntary decrease or complete cessation of

marketing to physicians"?

MR. ARBITBLIT: Object to reading a partial sentence.

MR. HERMAN: Okay. I will read the full sentence.

Q. (BY MR. HERMAN:) "Amidst national efforts to curb the overprescribing of opioids, our findings suggest that manufacturers should consider a voluntary decrease or complete cessation of marketing to physicians." Did I read that correctly?

A. You did.

Q. Okay. And is it your understanding that this article relates to marketing by manufacturers?

A. My understanding is that the data source as described in the Methods section says "pharmaceutical companies."

Q. Well, do you have an understanding --

A. The three top companies that you cited were three opioid manufacturers, but I have not looked into the Open Payments database in enough detail to know that every company included in the Open -- Open Payments database is a manufacturer.

Q. Sorry. So you don't know -- I mean, the recommendation certainly is about manufacturers, correct?

A. In -- in the Discussion section, it says there's a national effort to curb overprescribing and that one way to do that would be to suggest manufacturers cease marketing to physicians.

Q. Okay.

A. It does not preclude other efforts.

Q. Tell me everything you know about marketing by pharmacies.

MR. ARBITBLIT: Object to form. Vague. Overbroad.

A. Everything I know about -- if there's a specific document that you would like me to review, I can -- I can do that. Otherwise, I would prefer to stick to what is in my report.

Q. (BY MR. HERMAN:) Okay.

A. In terms of my general knowledge about marketing by pharmacies, pharmacies market all kinds of products.

Q. Do you know if any of these studies apply to pharmacies?

MR. ARBITBLIT: Objection. Vague.

A. I believe what I have testified is that what is written in the Methods section of this Hadland article is that the Open Payments database includes information from pharmaceutical companies. And I have not looked at every company that is in the Open Payments database. And that's as much information as I can -- I can give.

Q. (BY MR. HERMAN:) Sitting here today, do you know if any of the opinions you are giving about marketing are applicable to pharmacies?

MR. ARBITBLIT: Objection. Vague. Overbroad.

A. I think all of the opinions that I have given are applicable to all -- they are -- they are -- they are -- the opinions are what they are. And they are applicable -- for example, I say that there is overprescribing and oversupply. I think that certainly applies to pharmacies.

Q. (BY MR. HERMAN:) Okay. Sticking to marketing, I asked specifically about whether your opinions -- whether any of these studies about marketing relate to pharmacies.

MR. ARBITBLIT: Objection. Vague, interrupted the witness and misstates the prior question.

A. I think what I have written here is the amount of information that I have, which is that these articles apply to pharmaceutical company marketing. And I would have to look at the extent to which -- I don't know what companies are -- the totality of companies that are included in the Open Payments database.

Q. (BY MR. HERMAN:) So in the course of your work, you haven't analyzed the materials in your report to determine who is marketing? That is your testimony?

MR. ARBITBLIT: Object to the form. Argumentative.

A. Determine who is marketing? I don't know what you mean by "who is marketing."

Q. (BY MR. HERMAN:) Well, in the course of your work, you are offering opinions about marketing. In this report, you haven't analyzed the materials that you cite in your report to determine who is engaged in marketing?

MR. ARBITBLIT: Object to form. Vague. Overbroad.

Q. (BY MR. HERMAN:) True or false?

A. I have reviewed the epidemiological evidence and reported it in this report to the best

of my ability. And what I reported is that pharmaceutical companies are in the Open Payments database.

Q. But you don't know what "pharmaceutical companies" actually refers to, and you would agree with me that this article only discusses manufacturers, correct?

MR. ARBITBLIT: Objection. Compound.

A. What I can testify is that, in the Results section of this paper, three companies are mentioned, and those three companies are manufacturers.

Q. (BY MR. HERMAN:) And in the recommendation that the study makes at the end, it only mentions manufacturers, correct?

MR. ARBITBLIT: Objection. Misstates the record.

A. No, that is not correct. The sentence says that there are national efforts to curb overprescribing, which is not specific to manufacturers. And the second part of the sentence suggests that manufacturers curb marketing to physicians.

Q. (BY MR. HERMAN:) In an article about marketing to physicians, their "findings suggest

that manufacturers should consider a voluntary decrease or complete cessation of marketing to physicians." You don't agree that is only about manufacturers?

MR. ARBITBLIT: Object to form. Argumentative. Misstates the record.

A. I think I would consider the whole sentence together, which starts, "Amid national efforts to curb the overprescribing of opioids." And I think that that is a more general statement.

Q. (BY MR. HERMAN:) Okay. You don't -- you don't agree with me that this article that cites manufacturers, three manufacturers as the largest payors and then makes a recommendation only as to manufacturers is about manufacturers?

MR. ARBITBLIT: Objection. Asked and answered. Compound. Argumentative.

A. I think that is a narrow interpretation of the data.

Q. (BY MR. HERMAN:) Okay. You actually don't know, as you previously testified, what the data in the Open Source Payment reflects, correct?

MR. ARBITBLIT: Objection. Asked and answered.

A. I have -- sorry. I have not reviewed

every company that is in the Open Payments database.

Q. (BY MR. HERMAN:) Have you reviewed any companies?

A. I have reviewed the epidemiological literature, of which this article is one of several, and reported its results faithfully.

Q. Okay. So you made no effort to identify who was responsible for the marketing of opioids?

MR. ARBITBLIT: Object to form. Misstates the record. Argumentative.

A. The effort that I made was to review the evidence and report it, and that is what I have done in my report.

Q. (BY MR. HERMAN:) Well, tell me everything you know about pharmacies' marketing of prescription opioids.

MR. ARBITBLIT: Objection. Previously asked. Argumentative. Overbroad. Vague.

A. In my report, I discuss various marketing efforts, as they have been reported in the epidemiological literature. I'm not offering opinions about specific companies' marketing, as I

note in the report.

Q. (BY MR. HERMAN:) You don't know -- you don't know which companies engaged in which activities, if any at all, correct?

MR. ARBITBLIT: Objection. Vague.

A. I am not offering -- I -- in terms of what is reported in these articles, there are specific companies mentioned. And so to the extent that specific companies are mentioned in the epidemiological literature, that is what I feel like I have the expertise to report on.

But I am not offering opinions about specific pharmacy marketing.

Q. (BY MR. HERMAN:) All those companies that are specifically mentioned are manufacturers, correct?

A. The three companies mentioned in Hadland's 2018 are manufacturers.

Q. I meant -- I am -- I am talking in any article. Like we just looked at one where you discussed Purdue, correct? That is a manufacturer.

MR. ARBITBLIT: Object to form. Compound. Vague.

A. I would not offer testimony about every article. I can speak to each article at the

time.

Q. (BY MR. HERMAN:) Did you review those articles carefully before using them in your report?

A. I did.

Q. Do you recall any mention of marketing by pharmacies?

MR. ARBITBLIT: Object to form.

A. I would need to review each article again.

Q. (BY MR. HERMAN:) Okay. So sitting here today, you don't know what companies engaged in marketing activity?

MR. ARBITBLIT: Object to form.

A. Sitting here today, I can report on the companies that are specifically mentioned in these articles.

Q. (BY MR. HERMAN:) And those are all manufacturers?

MR. ARBITBLIT: Object to form. Asked and answered. Overbroad.

A. The company -- the three companies that I mentioned in Hadland 2018 are manufacturers. And we can look at the other Hadland articles to go through the companies that are mentioned in those

as well.

Q. (BY MR. HERMAN:) And the marketing activities that -- the studies you are looking at are marketing to prescribers, correct?

A. They are marketing to physicians.

Q. Okay. And when you are talking about factors that led to increased prescribing, you are speaking about the general population of prescribers, not specific prescribers, correct?

A. There is information on specific types of prescribers in various articles, but there was an overall increase in opioid prescriptions across many different types of prescribers, I guess. If that -- if I am -- I might be misunderstanding the question, so I am sorry if I am.

Q. I will try to do it a little differently.

You don't know what caused a particular prescriber to write a particular prescription, correct?

MR. ARBITBLIT: Object to form.

A. I have not evaluated particular prescribers.

Q. (BY MR. HERMAN:) Okay. You don't

know a particular prescriber's knowledge about the potential risks of prescription opioids, correct?

MR. ARBITBLIT: Object to form.

A. I can -- I can speak in generalities about what the epidemiological literature says about prescribers, but I have not evaluated any singular prescriber.

Q. (BY MR. HERMAN:) You don't know whether a particular prescriber saw marketing materials, correct?

A. I don't have any -- I don't have any expertise on particular prescriber, so I do not know whether they saw marketing materials.

Q. Okay. And I think you have already answered this, but you don't know what, if any, marketing materials doctors who prescribed opioids in Trumbull and Lake Counties saw, correct?

A. That's correct.

Q. Okay. Can I ask you to turn to Page 40 of your report? And can you see at the end of the first full paragraph where there's a reference to "'aggressive and highly'" -- it is a quote, "'aggressive and highly effective marketing tactics on the part of the pharmaceutical industry (manufacturers, distributors and pharmacies)'"?

A. Yes, I see that.
Q. And you cite to Reference 190 and specifically Section 719 for that proposition.
A. Yes.
Q. Okay.
(Exhibit 10 was marked for identification.)
MR. HERMAN: Can -- Jason, can we pull up -- what exhibit are we on, 9?
MR. ACTON: Yeah.
Q. (BY MR. HERMAN:) Can I ask you to open Exhibit -- CVS Exhibit 6, Professor Keyes? And Exhibit 9 [sic] is a document called "High and Rising Mortality Rates Among Working-Aged Adults." And is that what you referenced as Reference 190 in your report?
A. It is.
Q. Okay. And if I could ask you to turn to 7-19. And do you see where you pulled that quote from, there's a citation in support of it to an article by Kolodny, et al., 2015?
A. Page 7-19.
Q. Do you see at the top it says --
A. Oh, I was looking in the wrong section.

Q. Quoted at the top, "Aggressive and highly effective marketing tactics on the part of pharmaceutical industry (manufacturers, distributors, pharmacies)." And there's a citation to Kolodny et al. --

A. Yes.

Q. -- in support of that. Okay.

MR. HERMAN: Can I ask you, Jason, to pull up Exhibit 10 -- well, it's going to be Exhibit 10 --

MR. ACTON: 11.

Q. (BY MR. HERMAN:) Oh, Exhibit 11. And, Professor Keyes, can I ask you to open Exhibit -- CVS Exhibit 8?

A. I'm sorry. I -- the Kolodny article is citing actions of the legal and illegal drug suppliers and regulatory failures of government agencies.

Q. Well, I believe, though, it is also the only citation in support of "aggressive and highly effective marketing tactics on the part of the pharmaceutical industry (manufacturers, distributors, and pharmacies)"?

A. Oh, I see. In the second paragraph.

Q. Yeah. Okay.

A. Okay.

MR. HERMAN: Can we pull up that Kolodny article, if you could open CVS 8? And that is going to be Exhibit 11.

(Exhibit 11 was marked for identification.)

A. CVS 7-8 or CVS 8?

Q. (BY MR. HERMAN:) CVS 8.

A. Okay.

Q. Okay. And CVS 8 is an article entitled "The Prescription Opioid and Heroin Crisis: A Public Health Approach to an Epidemic of Addiction," and the authors are Andrew Kolodny, David T. Courtwright, Katherine Hwang, Peter Kreiner, John L. Eadie, Thomas W. Clark, and G. Caleb Alexander, and this was an article published January 12th, 2015; is that correct?

A. Yes.

Q. Okay. Are you aware that Professor Alexander has been retained by and identified as an expert witness by plaintiffs in this opioid litigation?

MR. ARBITBLIT: Object to form. Vague as to time.

A. Could you specify what you mean by

"this opioid litigation"?

Q. (BY MR. HERMAN:) Well, in the case that you are here testifying in today, the Trumbull and Lake County case.

MR. ARBITBLIT: Same objection.

A. I have -- I have been vaguely aware that Dr. Alexander has been -- I think I have supplied him with some estimates. And that is my knowledge of his involvement.

Q. (BY MR. HERMAN:) Okay. So as part of your work with the plaintiffs, you have provided Dr. Alexander estimates?

A. Yes.

Q. Okay. Are you aware that Professors Courtwright and Kolodny have been retained by and identified as expert witnesses by plaintiffs in other opioid litigation cases?

MR. ARBITBLIT: Same objection. Vague as to time. Misleading.

A. I have seen Dr. Kolodny's name in other litigation, and I don't recall seeing Dr. Courtwright.

Q. (BY MR. HERMAN:) Okay. Okay. And if I direct your attention to, "In addition to minimizing risks of OPRs, the campaign" -- well, I

direct your attention to 562, the bottom of the page. Do you see where it says, "In addition to minimizing the risks of OPRs, the campaign advanced by opioid manufacturers and pain organizations exaggerated the benefits of long-term opioid use"? Do you see that?

A. "In" -- yeah, "the campaign advanced by opioid manufacturers and pain organizations" -- yes, I see it.

Q. Okay. And that only discusses opioid manufacturers, correct?

MR. ARBITBLIT: Object to form. Misstates.

A. That sentence refers to "opioid manufacturers and pain organizations."

Q. (BY MR. HERMAN:) Well, okay. Does it discuss pharmacies?

A. That particular sentence or the article?

Q. Well, before quoting "High and Rising Mortality Rates Among Working-Age Adults" about aggressive and effective -- or marketing by manufacturers, distributors and pharmacies, did you look to see whether it or the article it cited provided any support for the idea that pharmacies

engaged in, quote/unquote, aggressive and effective marketing of prescription opioids?

MR. ARBITBLIT: Object to form. Argumentative.

A. Yes.

Q. (BY MR. HERMAN:) Okay. Tell me what in either of those discusses marketing by pharmacies.

MR. ARBITBLIT: Object to form.

A. In that sentence or the whole article?

Q. (BY MR. HERMAN:) Well, you said you checked. So if you could point me to where there's discussion of marketing by pharmacies, I would ask that you do so.

MR. ARBITBLIT: Object to form. Argumentative.

A. I'm not sure where -- I can read the article again.

Q. (BY MR. HERMAN:) Well, tell me everything -- I have asked you a couple of times now. I have asked you to tell me everything you know about marketing by pharmacies from this article or otherwise, and I haven't gotten a response.

MR. ARBITBLIT: Object to form. Argumentative. Misstates.

A. Yeah, I mean, just glancing over this article, it mentions opioid companies a number of times.

Q. (BY MR. HERMAN:) Do you know if those companies are pharmacies?

MR. ARBITBLIT: Object to form. Interrupting the witness.

A. I don't see specific pharmacies mentioned in this article. But there is discussion of a range of opioid companies, or companies that are involved in the distribution of opioids. And this article, as well as many others, have discussed the distribution of opioids as part of an oversupply problem.

Q. (BY MR. HERMAN:) Okay. Where does it discuss marketing -- I mean, you're -- it seems to me that you are changing the question. But where does it discuss marketing by pharmacies to support the idea that pharmacies engaged in aggressive and effective marketing?

MR. ARBITBLIT: Object to the form. Argumentative.

A. I -- so the sentence that is cited

with regard to the National Academies report is broader than just marketing activities. It includes flooding the market with highly addictive, yet deadly substances. And I think that the Kolodny article provides pretty solid evidence of the flooding of the market --

Q. (BY MR. HERMAN:) Well, that -- go ahead.

A. -- so it is an appropriate citation for that sentence.

Q. Well, if you're talking --

A. With regard to specific marketing activities, no specific marketing activities are discussed in this article, but a broad range of activities by these companies is discussed in the article. And there's discussion of marketing by various companies.

Q. But you would agree with me, I mean the sentence that you quote in your report is, "On the supply side, weak government regulations and aggressive and highly effective marketing tactics on the part of the pharmaceutical industry (manufacturers, distributors, pharmacies)," that neither of these sources provide support for the ideas that pharmacies engaged in aggressive and

highly effective marketing?

MR. ARBITBLIT: Object to form.

A. That -- the citation of the Kolodny article is a -- is a larger sentence. It is -- it is not just the --

Q. (BY MR. HERMAN:) Well, but I am asking you about the portion of the sentence that says "aggressive and highly effective marketing." You would agree with me that the Kolodny article does not provide support for the idea that the pharmacies engaged in highly effective and aggressive marketing, correct?

A. I would not agree with that broad of a statement.

Q. Well, what is your basis that the pharmacies engaged in aggressive and highly effective marketing?

A. My testimony is that the Kolodny article describes overall industry marketing and distribution practices that were deceptive and that the pharmacies would be included in that.

Q. Well, let's limit it to marketing. We will put aside your editorializing about distribution. But what -- I mean, the marketing example discussed, again, is Purdue. The only

campaign advance discussed is by opioid manufacturers and pain organizations. What are you basing your assertion that pharmacies engaged in -- that the Kolodny article discusses the fact that pharmacies engaged in any marketing, let alone aggressive and highly effective marketing?

MR. ARBITBLIT: Objection. Vague. Argumentative.

A. My testimony is the same as the previous question. I think, in citing the Kolodny article, there is discussion of a broad range of activities by companies.

Q. (BY MR. HERMAN:) Well, what --

A. And that is my -- that is the expertise that I am offering.

Q. Okay. But I want to zero in on the marketing aspect. I am only asking you about the activity of marketing.

A. Can you define what you mean by "marketing"?

Q. Well, what did you mean by it when you used it in your report and you cited this sentence in your report?

A. I -- what I meant by "marketing" is activities that increased the oversupply and

overprescription of opioids.

Q. Okay. And, I mean, when you are talking about marketing to physicians, what marketing activities were you aware of, if any, engaged in by pharmacies?

MR. ARBITBLIT: Object to form.

A. Neither the report, the National Academies article, or the Kolodny article specifies marketing to physicians when talking about marketing.

Q. (BY MR. HERMAN:) But your report --

A. That is a separate issue.

Q. I mean -- okay. Well, let's just talk about marketing generally. Are you redefining "marketing" to mean distribution, dispensing? Are you including those in marketing now?

I mean, I think "marketing" has a pretty -- I mean, what do you mean by "marketing"?

MR. ARBITBLIT: Object to form. Compound. Confusing. Vague.

A. Yeah, I am not -- what is the specific question?

Q. (BY MR. HERMAN:) Let's start on Page 14, "direct marketing to physicians." Are you aware of any activities by pharmacies that entail

direct marketing to physicians?

MR. ARBITBLIT: Object to the form.

A. Page 14 of my report?

Q. (BY MR. HERMAN:) Yes.

MR. ARBITBLIT: Object to form.

A. That goes back to the Hadland article and the testimony I have already provided about the Open Payments database.

Q. (BY MR. HERMAN:) Okay. So -- and your testimony was you don't know one way or another whether that relates to pharmacies?

MR. ARBITBLIT: Object to form.

A. We can go back and read the testimony. I mean, I didn't say I don't know one way or the other. What I said was that the Hadland article is based on the Open Payments databases, and that what is reported in the Methods section is that pharmaceutical companies are in the Open Payments database. I have not analyzed the Open Payments database to derive what industry each company that is in the Open Payments database is from.

Q. (BY MR. HERMAN:) Okay. And then on Page 33 it says, "exposure to pharmaceutical marketing" -- Page 33 of your report, "exposure to

pharmaceutical marketing and sales efforts" -- or -- it says, "association between exposure to pharmaceutical marketing and sales efforts with changes in prescribing." And do you know --

A. I mean, pharmacies are involved in opioid sales, are they not?

MR. ARBITBLIT: Wait for a question.

A. Sorry.

Q. (BY MR. HERMAN:) Well, I think it is talking about sales efforts with changing in prescriber behaviors, and that is what the studies you cite are about. So are you aware of pharmaceutical marketing efforts and sales efforts that change prescriber behavior that pharmacies engaged in?

MR. ARBITBLIT: Object to form.

A. Again, this -- I think the articles that are cited there refer to the Open Payments database. So my testimony would be the same, that the Open Payments database, from my understanding, includes pharmaceutical companies, and I am not -- I don't know all of the companies that are included in the database.

Q. (BY MR. HERMAN:) Okay. So sitting here today, you couldn't give an opinion one way or

another whether this relates to your opinions about marketing on Page 14 and Page 33 of your report relate to pharmacies?

A. I am not offering opinions about specific marketing activities of specific pharmacies or pharmacy chains. I am offering opinions about these articles in generality, in aggregate.

Q. Do you know if CVS engaged in any direct marketing activities to prescribers?

MR. ARBITBLIT: Objection. Vague.

A. Again, I am not offering opinions about CVS's marketing activities in -- specifically.

Q. (BY MR. HERMAN:) Okay. So that same answer would apply to Walmart, Walgreens, Rite Aid and Giant Eagle?

A. Yes.

MR. HERMAN: Okay. We have been going about an hour. Do people want to take a break?

A. Sure.

MR. ARBITBLIT: All right. We will break for like five minutes.

THE VIDEOGRAPHER: Stand by. We are

now off the record. The time on the video monitor is 1:52.

(Whereupon, a break was had from 1:52 p.m. until 2:01 p.m. EDT)

THE VIDEOGRAPHER: Stand by. We are now on the record. The time on the video monitor is 2:01.

Q. (BY MR. HERMAN:) Dr. Keyes, can I ask you to open 7-27, which will be Exhibit 12 for purposes of this deposition?

(Exhibit 12 was marked for identification.)

Q. (BY MR. HERMAN:) And do you have that, Doctor, please?

A. I am just opening it. The tape is --

Q. I saw you struggling a little bit. That is when I realized you didn't have it open.

Okay. Do you have it now?

A. I do.

Q. Okay. And so Exhibit 12 is an article entitled "Patterns of major depression and nonmedical use of prescription opioids in the United States." And you are one of the authors on this article, correct?

A. Yes.

Q. This was an article published in August 2015?

A. Yes.

Q. And can I direct your attention to Page 6, the last paragraph? And this article found that "Past-year drug use other than NMUPO and alcohol use disorder were the strongest factors associated with NMUPO alone, MDE alone and NMUPO plus MDE." That is what is read in here, correct?

A. Yes.

Q. And NMUPO means nonmedical prescription opioid use?

A. Nonmedical use of prescription opioids.

Q. And MDE means major depressive episode?

A. Yes.

Q. And can I direct your attention to Table 12 -- or Table 2? I apologize. And directing your attention to the section on adolescents, this table shows that adolescents who had any drug use other than nonmedical use of prescription opioids were 7.9 times more likely to have nonmedical use of prescription opioids alone, correct?

A. Let me just familiarize myself. Yes. Past any drug use other than nonmedical use of prescription opioids was associated with eight times higher odds of using prescription opioids nonmedically.

Q. Okay.

A. Without MDE.

Q. Okay. And adolescents who had any drug use other than nonmedical use of prescription opioids were 12.4 times more likely to have nonmedical use of prescription opioids and MDE?

A. That's correct.

Q. And adults who had any drug use other than nonmedical use of prescription opioids were 6.6 times more likely to have nonmedical use of prescription opioids alone, correct?

A. That's right.

Q. And adults who had any drug use other than nonmedical use of prescription opioids were 15.9 times more likely to have nonmedical use of prescription opioids and major depressive episodes?

A. Yes.

Q. You can set that aside. Can I ask you to open CVS 9? And this will be Exhibit 13.

(Exhibit 13 was marked for

identification.)

Q. (BY MR. HERMAN:) Sorry. I lost -- let me know when you have that open.

A. I do.

Q. And this is an article entitled "Psychoactive substance use prior to the development of iatrogenic opioid abuse: A descriptive analysis of treatment seeking opioid abusers," correct?

A. Yes.

Q. It is an article by Thomas Cicero and some other authors?

A. Theodore, but yes.

Q. Oh, that is. Thank you. Theodore Cicero. And if you look at the abstract, it says, "Physicians are frequently thought to be major -- be a major source of opioids diverted for nontherapeutic purposes, largely because it is so difficult for them to discern when patients -- which patients might abuse them.

"In this study, we sought to determine whether those who were first exposed to opioids through a physician's prescription and subsequently developed a substance use disorder had a history of using psychoactive drugs prior to

abusing opioids." Correct?

A. Yes.

Q. And if you look at the introduction, it says, "Healthcare professionals who write opioid prescriptions for acute and, particularly, chronic pain have to consistently balance two often nagging considerations. First, since there is no tool to precisely gauge the presence or severity of the highly subjective experience of pain, physicians must exercise their professional judgment as to whether opioids are warranted or appropriate.

"And, second, the more troubling point is it is very difficult for physicians to determine which patients are currently abusing opioids or are at risk for abuse."

Did I read that correctly?

A. You did.

Q. And do you agree with the statements in this introduction that physicians have to consistently balance the two often nagging considerations that are discussed here?

MR. ARBITBLIT: Object to form, vague.

A. I would agree that these are two among many considerations that healthcare

professionals need to make.

Q. (BY MR. HERMAN:) And do you agree that the presence or severity -- the determination of the presence or severity of pain is a highly subjective determination?

A. Yes, I agree.

Q. And do you agree that it is difficult for physicians to determine which patients are currently abusing opioids or are at risk for abuse?

A. I wouldn't say that as a blanket statement. Sometimes it can be difficult, and sometimes it is not difficult.

Q. And can I ask you to turn to Page 2, "Discussions and Conclusions"? And do you see where it says, "The results of this study indicate that only four percent of those who experienced their first opioid via physician's prescription were truly drug naïve.

"Rather, more than ninety-five percent had significant psychoactive drug experience prior to being prescribed their first opioid, a drug with well established mood altering effects.

"Two aspects of the data seem noteworthy. First, while nearly our entire sample

had used alcohol, nicotine and marijuana before their initial opioid prescription, seventy percent had experience with other types of drugs. And second, on average, four to five different types of drugs were used prior to initial opioid exposure from a prescription"?

Do you see that?

A. I see that.

Q. Did I read that correctly?

A. You read it correctly.

Q. Any reason you would not expect these figures to apply to individuals prescribed prescription opioids in Lake and Trumbull County?

MR. ARBITBLIT: Object to form. Vague. Overbroad.

A. Yes. This is not a general population sample. These are people in treatment for prescription opioid use disorders. So these results would not apply to the general population of Lake and Trumbull County.

Q. (BY MR. HERMAN:) Would you believe they would apply to the people in need of treatment for opioids in Lake and Trumbull County?

MR. ARBITBLIT: Object to form.

A. That is not what this sample is.

This sample is individuals who are in treatment.

Q. (BY MR. HERMAN:) Patients entering one of one hundred and twenty-five drug treatment programs across the country for opioid abuse were asked to provide detailed history, is that what you were referring to, was people entering into treatment?

A. Right.

Q. Okay. And so that is a population of people who are in need of treatment, correct?

MR. ARBITBLIT: Object to form.

A. They are people who are in treatment. There are people who are in need of treatment or not in treatment. So it wouldn't comprise the entire population of people who need treatment.

Q. (BY MR. HERMAN:) But you would agree with me that it would comprise a subset of the population in need of treatment that is seeking treatment at that time, correct?

A. I don't understand the question.

Q. Well, let me ask it this way: People in treatment are a subset of the total population of people who need treatment, correct?

A. Yes.

Q. And so do you have any reason to

believe that these statistics for a population in treatment would not generalize to the population in need of treatment?

MR. ARBITBLIT: Object to form.

A. I have not analyzed that data. I don't know whether these results generalized all those who are in need of treatment.

Q. (BY MR. HERMAN:) Well, do you believe that a very small percentage of people who experience their first opioid via physician prescription are truly drug naïve?

MR. ARBITBLIT: Object to form. Misstates the record.

MR. HERMAN: Well, let me strike that.

Q. (BY MR. HERMAN:) This study found the results of this study indicate that only four percent of those who experienced their first opioid via physician's prescription were truly drug naïve, correct?

MR. ARBITBLIT: Object to form.

A. Those are the results of the study.

Q. (BY MR. HERMAN:) And so do you believe that those people who experienced their first opioid via physician prescription who end up

needing treatment are truly drug naïve?

MR. ARBITBLIT: Object to form. Misstates the record.

A. That question is not what this study analyzed.

Q. (BY MR. HERMAN:) That is what this study found, correct?

MR. ARBITBLIT: Object to form. Misstates the record.

A. No, it is not what the study found. The study found that among this population of people in treatment in -- from 2010 to 2015, four percent of those who experienced their first opioid via physician's prescription had not used one of the drugs that were assessed in this study.

THE REPORTER: That were what in this study?

A. Had not used one of the drugs that were assessed in this study.

Q. (BY MR. HERMAN:) Do you have any reason to believe that the patient population that ends up needing treatment who experienced their first opioid via physician's prescription were truly drug naïve?

MR. ARBITBLIT: Objection, vague.

A. Yes.

Q. (BY MR. HERMAN:) What is your basis for saying that the patient population that ends up needing treatment who experience their first prescription opioid through a physician prescription was truly drug naïve?

A. This study concludes that four percent who experience their first opioid via a physician's prescription had not used one of the drugs that were assessed in this study. Given the millions of people who have their first opioid, among those who end up going to treatment, four percent is a lot of people.

Q. Well, are you agreeing, though, that the four percent would generalize to the population of people who need treatment for --

A. I would need to evaluate --

THE REPORTER: I'm sorry. Y'all spoke over each other. I couldn't --

A. I apologize. I interrupted.

Q. (BY MR. HERMAN:) Putting aside whether four percent of the population is a lot of people, do you believe that the four percent figure in this study would be generalizable to the population that ends up needing treatment?

MR. ARBITBLIT: Object to form. Speculative.

A. I would prefer more study. I mean, generalizing from one study is not typically what we do in epidemiology.

Q. (BY MR. HERMAN:) Okay.

A. So to evaluate the generalizability of this number, I would need to know what population we are generalizing to, what information we have about their demographic characteristics, that you would just need to consider all of those factors.

Q. And you don't know one way or another whether the people in Lake and Trumbull County who might need treatment who experienced their first opioid via a physician's prescription were truly drug naïve?

MR. ARBITBLIT: Object to form.

A. The people in this study were in treatment, not might need treatment. And the extent to which the four percent would generalize to Lake and Trumbull County, I would need -- I would need further information to evaluate the generalizability.

Q. (BY MR. HERMAN:) You can't --

whether this study numbers would apply to Lake and Trumbull County, you would need to know -- am I understanding it correctly you would need to know more about the population and characteristics of the people in Lake and Trumbull County?

MR. ARBITBLIT: Objection.

A. Those who are in treatment.

Q. (BY MR. HERMAN:) And the issue is, this study was done on a population, and you don't know if that population is reflective of the Lake and Trumbull County population? Am I understanding you correctly?

MR. ARBITBLIT: Object to form. Misstates the record.

A. That is not my testimony.

Q. (BY MR. HERMAN:) Well, what am I --

A. My testimony is that in order to engage in generalizability -- it is not that I don't know. It is that I haven't evaluated the extent to which the treatment utilization population of this particular sample is similar or different than the treatment-using population of Lake and Trumbull County.

Q. Okay. And that is in part because you haven't evaluated the treatment-needing

population of Lake or Trumbull County, correct?

MR. ARBITBLIT: Object to form.

A. I have not evaluated the generalizability of this study to that population.

Q. (BY MR. HERMAN:) Well, I am asking a slightly different question. I mean, have you evaluated the specific treatment-needing population of Lake and Trumbull County?

A. I believe that is included in my report. I have provided a number of estimates about that population.

Q. But you don't know the characteristics of that population, for example, whether they are truly drug naïve, correct?

MR. ARBITBLIT: Object to form.

A. If the population is in treatment, then they certainly are not drug naïve.

Q. (BY MR. HERMAN:) Well, drug naïve before they encounter prescription opioids.

MR. ARBITBLIT: Object to form. No question pending. There's no question pending. Wait for a question. It is a statement.

Q. (BY MR. HERMAN:) Professor Keyes, have you evaluated the characteristics of the population in Lake and Trumbull County that is in

need of treatment specifically -- well, I will ask that question first.

MR. ARBITBLIT: Object to form.

A. Wait. I'm sorry. Is there a question?

Q. (BY MR. HERMAN:) Have you evaluated the characteristics of the population in Lake and Trumbull County in need of treatment?

A. Yes. I have evaluated some characteristics that are included in my report.

Q. Well, all those are estimates, correct?

MR. ARBITBLIT: Object to form.

A. I mean, statistics are an estimate.

Q. (BY MR. HERMAN:) Okay. And you don't know anything about -- for example, let's take your estimate of NAS, potential NAS births. You estimate that there are six NAS births in Lake County, I believe, in Lake County in -- well, one of the years. So I am going to ask you to assume that you provide an estimate of six NAS births in one of the years. Okay. Are you with me?

MR. ARBITBLIT: Object to form.

A. I am finding the page of the report. I believe you are on Page 51.

Q. (BY MR. HERMAN:) I am just asking you to assume that I have your numbers correct, that in one of the years in one of the counties you estimate there were six NAS births. Okay. Are you following what I am asking you to assume?

MR. ARBITBLIT: Object to form.

A. Yes.

Q. (BY MR. HERMAN:) Okay. As to those six mothers who gave birth, do you have any information about what drugs those six mothers used?

A. I don't have any information about those six mothers.

Q. All right. So you don't know whether the NAS birth, for example, was the result of legitimately prescribed opioids versus illicit opioids?

MR. ARBITBLIT: Object to form.

A. I do provide estimates of that in various drug-using populations for which there is a broader range of studies that we can use to generalize to inform that question. So the extent to which medical versus nonmedical opioids are used in opioid-using populations, there is a sufficient number of studies that we can provide more

generalizable estimates.

Q. (BY MR. HERMAN:) Okay. But as to those estimated six mothers, you don't actually -- it is an estimate. You don't know anything about those individuals, their drug use trajectory, whether they used a prescribed or illicit opioid, correct?

MR. ARBITBLIT: Object to form. Vague. Compound.

A. For the six individual -- well, there's not -- the babies are what is reported in the table.

Q. (BY MR. HERMAN:) Sure. But it would be the mother's drug use that would result in an NAS birth, correct?

A. Right. I have not evaluated the particular drug use history of any mother in Lake and Trumbull County.

Q. Do you know how many pharmacies existed in Lake or Trumbull County that dispensed prescription opioids?

A. No.

Q. So do you have any way of knowing whether any of the estimated births in Lake or Trumbull County in your chart were caused by

prescription opioids dispensed by a pharmacy that is a defendant in this litigation?

MR. ARBITBLIT: Object to form.

A. I can provide expertise on the estimated use of prescription opioids among pregnant women in that area.

Q. (BY MR. HERMAN:) Okay. Is the answer to my question no, you have no way of knowing whether any of the estimated NAS births in Lake and Trumbull County were caused by prescription opioids dispensed by a defendant in this case?

MR. ARBITBLIT: Object to form.

A. That is not my testimony. I think what is in the report provides information that can be used to infer causation with regard to prescription opioid use that would be dispensed by a pharmacy.

Q. (BY MR. HERMAN:) But you don't know if it was dispensed -- how would you figure out if one of those births, one of your estimated births was caused by a prescription opioid dispensed by CVS?

MR. ARBITBLIT: Object to form.

A. One could estimate that, given the

distribution of CVS pharmacies in the area.

Q. (BY MR. HERMAN:) But to actually know whether a birth was caused -- an NAS birth was caused by a prescription opioid dispensed by CVS, one of six births, you would have to actually show, wouldn't you, that that mother came in contact with an opioid dispensed by CVS, correct?

MR. ARBITBLIT: Object to form. Calls for a legal conclusion.

A. I would perform epidemiology using the methods that I outlined in the beginning of my report to estimate causation.

Q. (BY MR. HERMAN:) Can you -- can you point to -- well, can you explain to me how you would go about figuring out if one of those six NAS births was caused by a particular pharmacy in Lake or Trumbull County?

A. So I would do a risk factor analysis, as I have outlined in the beginning of the report, which is how we analyze data in epidemiology. So you would estimate associations using regressions, controlling for confounding factors. You know, in recent years, the number of NAS births in Lake and Trumbull County is quadruple the six that you cite in 2008. So you certainly would have more

statistical power if you used more recent years.

Q. Okay. And is it likely that a prescription opioid dispensed in 2010 led to an NAS birth in 2018?

A. Yes.

Q. How would you go about figuring out if a prescription opioid dispensed in 2010 led to an NAS birth in 2018?

A. We know very well that the dose and duration of prescription opioid use is associated with the development of opioid use disorder and prolonged opioid use disorder. And so you would examine the onset and duration of prescription opioid use.

Q. By that specific individual?

MR. ARBITBLIT: Object to form.

A. I guess I am not understanding the question.

Q. (BY MR. HERMAN:) Well, you would need to know something about the dosage taken by the individual, correct?

A. The hypothetical here is about a hypothetical what, single person? I would do a risk factor analysis of, you know, a population, which is what we do in epidemiology.

Q. Well, you are estimating that six people had an NAS birth. And so I am saying okay, I want to know whether a prescription opioid dispensed in years before that led to that birth. And you said well, you would need to know something about the dose and duration.

And so I am asking you, you would need to know about that specific individual's drug use trajectory, correct?

MR. ARBITBLIT: Objection. Vague. Compound. Misstates the record.

A. There are a wide variety of sources that one could use to provide a causal analysis, including individual history as well as group history that could be inferred to the individual.

Q. (BY MR. HERMAN:) Can drugs other than prescription opioids cause NAS?

A. Can drugs other than prescription opioids?

Q. Yes.

A. Yes.

Q. Can drugs other than opioids generally cause NAS?

A. NAS is certainly the predominant -- opioids are certainly the predominant cause of NAS

birth outcomes. And there's some discussion about whether symptoms that occur in neonates that are caused by other drugs are the same syndrome as NAS. So it is a little bit more of a complicated question than a yes or no, but it is possible, I guess I would say.

Q. Okay. Can an NAS birth be caused by use of an illegal opioid, like heroin?

A. Yes.

Q. Fentanyl?

A. Yes.

Q. Would the use of heroin make it more likely that someone would have an NAS birth?

MR. ARBITBLIT: Objection. Vague.

A. More likely than what?

Q. (BY MR. HERMAN:) Well, more likely than the use of acute dosage of a prescription opioid.

MR. ARBITBLIT: Objection. Vague. Incomplete hypothetical.

A. It would -- it would depend on the dose and duration of use. So it is a dose response relationship for both.

Q. (BY MR. HERMAN:) Okay. All things being equal in terms of dosage, would someone who

used heroin be more likely to have an NAS birth or someone who used a prescription opioid?

MR. ARBITBLIT: Objection, vague. Incomplete hypothetical.

A. If the same amount of opioid is consumed, I would say that they are approximately equal.

Q. (BY MR. HERMAN:) Okay. And would your answer be the same for illicit fentanyl?

A. The potency of fentanyl is much higher than that of heroin. So in a hypothetical world where the potencies were the same, then the risk would be similar.

Q. But so because the potency of fentanyl is higher, if someone was using illicit fentanyl, would they be more likely to have an NAS birth?

MR. ARBITBLIT: Object to form. Incomplete hypothetical.

A. It depends on the potency of what you are comparing it to.

Q. (BY MR. HERMAN:) Can an NAS birth occur as a result of an individual taking prescribed opioid medications?

A. Yes.

Q. Can an NAS birth occur as a result of an individual taking medically-assisted treatment medications?

A. Yes.

MR. HERMAN: What exhibit are we on?

Q. (BY MR. HERMAN:) Can I ask you, Professor Keyes, while we are figuring out the exhibit number, to take out what is CVS 7-23. And this is going to be Exhibit 14.

(Exhibit 14 was marked for identification.)

Q. (BY MR. HERMAN:) Do you have it, Professor Keyes?

A. I do.

Q. Okay. This is an article entitled "Associations of Nonmedical Pain Reliever Use and Initiation of Heroin Use in the United States." And it is authored by Pradip Muhuri; is that correct?

A. Uh-huh, yes.

Q. Okay. And this is -- this study by Muhuri -- am I pronouncing that right?

A. I believe so.

Q. This study by Muhuri is one you rely on in your report?

A. It is.

MR. ARBITBLIT: Counsel, I don't mean to interrupt, but can we have a representation that whatever you are going to ask about Muhuri has not been covered in previous depositions? This article has appeared so many times in so many depositions that it is hard to imagine there's anything new to say about it.

MR. HERMAN: Well, I think I am going to ask some new questions, but I may touch on some things that were done before. But I will try to keep that to a minimum.

Q. (BY MR. HERMAN:) I'm not sure I got an answer to my question. It is a high-quality research study?

MR. ARBITBLIT: Object to form.

A. I believe it is a reliable study.

Q. (BY MR. HERMAN:) And the lead authors are at SAMHSA?

A. The affiliation of the authors is not on the title page, so I actually don't know.

Q. Well, up at the top do you see where it says at least the study was put out by SAMHSA? You would agree with that?

A. Yes.

Q. And that is a substance abuse and mental health administration?

A. Yes.

Q. That is a leading federal agency for research on substance abuse?

MR. ARBITBLIT: Objection.

A. I don't -- I don't have any information to know whether it is the leading federal agency. NIDA is also a fairly prominent federal agency so --

Q. (BY MR. HERMAN:) Can we agree that it is one of the leading federal agencies for research on substance abuse?

A. I think I would be comfortable testifying that it is a federal agency for research on substance abuse.

Q. Okay. And they are relying on data from the National Survey on Drug Use and Health?

A. Yes.

Q. And that is data that is collected by the federal government?

A. Yes.

MR. ARBITBLIT: I'm going to object that none of this seems new to me, Counsel. It is all repetitive.

MR. HERMAN: Well, I am just laying a little background. I think I would ask for a little time.

Q. (BY MR. HERMAN:) All right. And if you look at Page 3 under "Data and Methods," they have been collecting data since 1971. Do you see that?

A. Yes.

Q. And for this study, the total sample size, if you look a couple of sentences in, was six hundred and nine thousand -- six hundred and nine thousand people considered at risk for heroin initiation; is that correct?

A. Yes.

Q. Then it says in the parenthetical "representing an annual average of approximately a hundred and fifty-five million individuals."

A. Yes.

Q. And that is a large sample, you would agree?

A. Yes, it is a large sample.

Q. In epidemiology, large samples generally give you better data?

MR. ARBITBLIT: Object to form,

vague.

A. I would not make that conclusion across the board.

Q. (BY MR. HERMAN:) Well, other things being equal, a larger sample gives you better data than a smaller one, correct?

MR. ARBITBLIT: Object to form, vague.

A. A larger sample provides more statistical precision, but the data are not necessarily better.

Q. (BY MR. HERMAN:) And then it says there was a total sample size of five hundred and twenty-four thousand people at risk for initiating NMPR use. Do you see that?

A. I do.

Q. And NMPR stands for nonmedical pain reliever, correct?

A. Correct.

Q. And in the parenthetical there, it says that represented an annual average of approximately a hundred thirty-two million persons?

A. Yes.

Q. And that is also a large sample?

MR. ARBITBLIT: Object to form.

A. That is a large sample.
Q. (BY MR. HERMAN:) And this study found that 79.5 percent of people that started using heroin had prior nonmedical pain reliever use, correct?
A. Is that Table 5?
Q. Well, if you look at, for example, the abstract and if you look a couple sentences up from the bottom, it says four out of five recent heroin initiates, 79.5 percent previously used NMPR.
A. So your question was?
Q. The study found that 79.5 percent of people who started using heroin had prior nonmedical prescription opioid use?
A. So those were recent heroin initiates. So it is not all, all individuals who use heroin. But among recent heroin initiates, 79.5 previously used pain relievers nonmedically.
Q. Okay. And NMPR means using opioids that weren't prescribed to you or only for experience or feeling you got from using the drug in this study? Do you recall that?
MR. ARBITBLIT: Object to form.
A. Yes.

Q. (BY MR. HERMAN:) And if I could direct you to Table 3.

A. Table 3, yes.

Q. And that has got four -- well, Table 3 shows data in that Muhuri reported about people in the study who started using heroin, correct?

A. Yes.

Q. And there are four columns. In the fourth column at right shows data for the full time period the authors looked at, 2002 to 2011?

A. Yes.

Q. And if you go down to the bottom, you see that 79.5 percent of the people who started heroin had prior NMPR use. Do you see that?

A. I see that.

Q. And right above that you see that 20.5 percent of people who started using heroin had no prior NMPR use?

A. I see that.

Q. In the same box, you see that 1.1 percent of people who started using heroin not only had no prior NMPR use, they had no prior illicit drug use?

A. Yes.

Q. And right below that you see that 19.4 percent of the people who started using heroin did not have prior NMPR use before they started using heroin but they did have prior use of other illicit drugs?

A. Yes.

Q. And going down to the next box, that is the box for people who had NMPR use before they started heroin, right?

A. Can you say that question again?

Q. Going down to the next box, we see the people who had NMPR use before they started heroin.

A. Yes.

Q. And you see that zero percent of the people who started using heroin had only prior NMPR use but no other illicit drugs?

A. Yes.

Q. And 79.5 percent of people who started using heroin had both prior NMPR use and prior use of other illicit drugs?

A. That is what the table says, yes.

Q. Everyone in the study who used heroin after misusing prescription opioids also had a history of using other illicit drugs, correct?

A. That is correct.
Q. And if we look at the people who started using heroin and want to know how many had prior use of illicit drugs other than prescription opioids, we could add up the two numbers Muhuri gives, 19.4 percent and 79.5 percent, correct?
MR. ARBITBLIT: Object to form.
A. This is -- just to qualify, these are recent heroin initiators and prior use of the illicit drugs that were assessed in the survey. But with those two qualifications, yes, you would add up those two percentages.
Q. (BY MR. HERMAN:) Okay. Those are the statistics, though, for the data they looked at for 2002 to 2011, correct?
A. Yes.
Q. And. So Muhuri's data shows that of people that started using heroin, 98.9 percent have prior illicit drug use other than prescription opioids.
MR. ARBITBLIT: Object to form.
A. In these data for these individuals with recent heroin initiation, 98.9 percent had a prior illicit drug use as well.
Q. (BY MR. HERMAN:) And can I ask you

to turn to Figure 6? It is on Page 11.

A. Yes.

Q. Okay. This figure breaks up people who started using heroin into three groups, correct?

A. Yes.

Q. The first bar is for a group who started using heroin after misusing prescription opioids, and they also showed dependence or abuse of prescription opioids in the year before they started using heroin, correct?

A. Correct.

Q. And dependence and abuse is based on definitions in DSM4?

A. That is right.

Q. Okay. And that is a standard reference work for diagnosing substance abuse conditions?

MR. ARBITBLIT: Objection. Time. Vague.

Q. (BY MR. HERMAN:) I think you nodded, Professor Keyes, but I think we need a verbal --

A. The DSM4 is commonly used in research for diagnosis.

Q. For diagnosing substance abuse

conditions?

A. Yes.

Q. And this data shows that people who started heroin, 31.3 percent of them had misused prescription opioids and in the year before starting heroin were abusing or dependent on prescription opioids under the DSM4 definition, correct?

A. Among -- yes, among those who started heroin, 31.3 percent had prior use in the past year abuse/dependence of pain relievers.

Q. Okay. And the second bar is people who started using heroin after misusing prescription opioids but in the year before starting heroin weren't showing dependence or abuse of prescription opioids, correct?

A. Yes.

Q. And this shows that 48.2 percent of people who started heroin had misused prescription opioids but in the year before starting heroin weren't abusing or dependent on prescription opioids under the DSM4 definition, correct?

A. Yes.

Q. And the third bar shows that 21.5 percent of people who started heroin had no prior

misuse of prescription opioids, right?

A. Yes.

Q. Okay. In your report, you recognize the people who transition from misuse of prescription opioids to heroin is relatively small, correct?

MR. ARBITBLIT: Object to form.

A. The transition probability is small. Not the number of people. The number of people is quite large.

Q. (BY MR. HERMAN:) Okay. But the percentage of people who transition from prescription opioids to heroin is relatively small, right?

MR. ARBITBLIT: Object to form. Vague.

A. Among people who use prescription opioids, either prescribed or nonmedically, the proportion that transition to heroin is relatively small. But it translates to a large number because of the commonality of the exposure.

Q. (BY MR. HERMAN:) Okay. Muhuri found that in five years after people started misusing prescription opioids, 3.6 percent of them started using heroin, correct?

A. Yes.
Q. And so after five years, 96.4 percent of people misusing prescription opioids had not tried heroin?
A. In this sample, yes.
Q. And those figures are for people who use prescription opioids nonmedically, correct?
A. Not exactly. The national household survey in these years did not ask about medical use. So there's a large overlap between medical and nonmedical users of prescription opioids. And so a large portion of these nonmedical users had also likely used medically or from a doctor's prescription --
Q. Okay. But the 3.6 is of nonmedical prescription, non-medical pain reliever initiates, correct?
MR. ARBITBLIT: Object to form. Vague. Misstates.
Q. (BY MR. HERMAN:) Well, I will direct your attention to the abstract. And do you have that in front of you?
A. I do.
Q. Only 3.6 percent of NMPR initiates had initiated heroin use within the five-year

period following first nonmedical prescription, nonmedical pain reliever use. Right?

A. Yes. That is what the abstract states. I just want to make clear for the record that they didn't -- it is not nonmedical use only. It is this population of people, there's a large overlap with medical use as well, which was not assessed in the survey.

Q. Do you know what percentage of people prescribed opioids use nonmedically?

A. I believe there's a citation to that. I can pull it up. Most people who use nonmedically have also used medically. And in the reverse --

Q. Okay.

A. -- the -- I have a citation of that. I will pull it up. I don't think I have the exact figure, but if you would like to pull up the paper, I am sure we can pull up the paper that would give you that information.

Q. Well, why don't you just tell me what paper you think provides that information.

A. McCabe, "Medical Use and Misuse of Prescription Opioids in U.S. 12th Grade Youth" would provide some of that information. And then also by McCabe, "Trends in Medical and Nonmedical

Use of Prescription Opioids Among U.S. Adolescents: 1976 to 2015."

Q. Okay. Let's maybe keep this simple. You would agree with me that the number of people who use prescription opioids medically is larger than the number of people who use prescription opioids nonmedically, correct?

A. Yes.

MR. HERMAN: We have been going about an hour. Do people want to take another quick break?

THE VIDEOGRAPHER: Stand by.

THE REPORTER: Yes.

THE VIDEOGRAPHER: We are now off the record. The time on the video monitor is 2:52.

(Whereupon, a break was had from 2:52 p.m. until 3:02 p.m. EDT)

THE VIDEOGRAPHER: We are now on the record. The time on the video monitor is 3:02.

Q. (BY MR. HERMAN:) Dr. Keyes, can I ask you to open up what is CVS 7-22.

MR. ARBITBLIT: What exhibit is this again?

MR. HERMAN: This is going to be Exhibit 15.

(Exhibit 15 was marked for identification.)

THE REPORTER: Hey, Steve, when you are saying 722, is it 7-22 or, all together, 722?

MR. HERMAN: 7-22.

Q. (BY MR. HERMAN:) Dr. Keyes, do you have that?

A. I do.

Q. And is Exhibit 15 an article entitled "Initiation Into Prescription Opioid Misuse Among Young Injection Drug Users"; is that correct?

A. It is.

Q. And this is an article that you cite in your report at Reference 176?

A. Yes.

Q. Can I ask you to turn to Page 4 of the section Initiation Into Prescription Opioid Misuse.

A. Yes.

Q. Okay. And do you see where it says, "Initiation of opioid misuse typically followed first use of alcohol, marijuana and prescription stimulants and preceded initiation of harder drugs, such as cocaine, methamphetamine and heroin?"

A. I see that, yes.

Q. And did I read that correctly?
A. You did.
Q. And if you go to the first page, Methods, for this study, they recruited fifty individuals ages sixteen to twenty-five who were injection drug users who had misused prescription opioids at least three times in the past three months, correct?
A. Yes.
Q. And so those characteristics mean that a hundred percent will misuse prescription opioids?
MR. ARBITBLIT: Object to form.
A. There were three eligibility criteria: Eighteen to twenty-five years old, misused a prescription drug -- it doesn't say opioids in particular -- and injected a drug within the past three months.
Q. (BY MR. HERMAN:) Okay. So a hundred percent will have misused a prescription drug?
A. Yes. It says opioids, tranquilizers or stimulants.
Q. And a hundred percent will be injection drug users?
A. Yes.

Q. And can I ask you to go to Table 2? Well, actually, let me ask you this first: On Page 4, right back where we were before, do you see where it says, "over four-fifths (N=43) initiated opioid misuse prior to heroin, which occurred two years earlier on average"?

A. I do.

Q. Okay. And what that is saying is that eighty-six percent had misused prescription opioids before they used heroin, just sequentially, correct?

MR. ARBITBLIT: Object to the form.

A. That's right.

Q. (BY MR. HERMAN:) And on average, that misuse occurred two years earlier than the person -- before when the person began using heroin?

A. Yes.

Q. If you go to Table 2, Table 2 lists a number of substances, and it has got three columns, and the last column shows the total percentage of the population in the study that had used the substance listed, correct?

A. Yes.

Q. So for the first one, it shows that a

hundred percent of the population in the study had misused marijuana, right?

A. That is right.

Q. And a hundred percent had misused alcohol?

A. Yes. Used alcohol.

Q. And eighty-two percent had used stimulants?

A. Yes.

Q. Okay. And then a hundred percent had used opioids, presumably prescription opioids and heroin, correct?

A. That's right.

Q. And then ninety-eight percent had used cocaine?

A. Yes.

Q. Ninety-four percent had used mushrooms?

A. Yes.

Q. Ninety-two percent had used tranquilizers?

A. Yes.

Q. Ninety-six percent had used ecstasy?

A. Yes.

Q. Eighty-six percent had used crack?

A. Yes.
Q. Okay. You can set that aside. And can I ask you to open up 7-21. This will be Exhibit 16.
Do you have it, Professor Keyes?
(Exhibit 16 was marked for identification.)
A. I do.
Q. (BY MR. HERMAN:) So Exhibit 16 is an article titled "Injection and Sexual Activity [sic] HIV/HCV Risk Behaviors Associated With Non-Medical Use of Prescription Opioids Among Young Adults in New York City"; is that correct?
A. That's correct.
Q. And this is another article you cite in your report?
A. I do. Do you know the citation number?
Q. It is 164.
A. Yeah.
Q. And if you go to Page 3 and look at the Methods section, this was a study that involved forty-six New York City young adults ages eighteen to thirty-two who engaged in non-medical prescription opioid use who were recruited for

individual interviews. "Twenty-three participants were referred by service providers (drug treatment programs, an outreach programs for young injectors, key informants, other research projects). And the remaining twenty-three were recruited via chain referral from other participants." Is that right?

A. That's right.

Q. And if you look at Page 15 and the last paragraph, do you see the sentence -- it is the second sentence that begins "Because this is a qualitative study based on interviews conducted with a relatively small number of participants who were sampled via non-probabilistic methods, the results are not intended to be generalizable to all young adult non-medical PO users." Do you see that?

A. I do.

Q. And that is some of what I think you were talking about earlier that you have to look at the population and what was being looked at to know whether the results would generalize to a larger population, correct?

MR. ARBITBLIT: Object to form.

A. There were a number of considerations with respect to generalizability. And population

comparability is one part of what we would evaluate. The other part would be the strength and variety of the evidence that is being offered to generalize.

Q. (BY MR. HERMAN:) Okay. And then if you go a little further down, they say, "We used quantitative data to precisely characterize our data, not to make statistical inferences about a larger population." Do you see that?

A. I do.

Q. And do you see on the next page, the study says, "Similarly, since the majority of study participants engaged in regular daily or nearly daily PO use, the behaviors and experiences of more casual, sporadic PO misusers may be underrepresented"?

A. I see that.

Q. And I read that correctly?

A. Yes.

Q. Can I ask you to turn to Page 5? And after the first block quote, do you see where it says, "Early PO use [sic]" -- and PO means prescription opioid, correct?

A. Prescription opioid.

Q. "Early PO misuse was typically

described as taking place within a normative peer context in which poly-drug and poly-pharmaceutical use was widely accepted. Some participants spoke of attending pill parties." Do you read that?

A. Yes. The rest of the sentence says, "where prescription opioids were used concurrently with benzodiazapines, prescription stimulants and marijuana."

Q. What is your understanding of normative peer context?

MR. ARBITBLIT: Object to form.

A. In terms of how the authors are using it in this sentence? Or a broader --

Q. (BY MR. HERMAN:) Sure. How they are using it in this sentence.

A. I would -- I would point to how the youth uses it in their quotation. That it was a gathering of four to fifteen people.

Q. Okay. And the context was one in which, among this population, poly-drug use and poly-pharmaceutical use was widely accepted, correct?

A. In this sample, the authors report that poly-drug and poly-pharmaceutical use was widely accepted.

Q. And if you look at the block quote above that, it is describing, from one of these interviews, someone said, "I first used opiate painkillers when I was seventeen. It was very simple. Basically somebody (stepfather) in my household had a massive back surgery. He didn't really like the way they made them feel, so they were just sitting, you know, sort of around the house. He would get them filled and never take them and never seemed to notice they were missing." Did I read that correctly?

A. Yes.

Q. And do you believe that it is appropriate for a doctor to prescribe prescription opioids for a massive back surgery?

MR. ARBITBLIT: Object to form.

A. It would depend on the context.

Q. (BY MR. HERMAN:) Okay. And -- well, in this scenario, what this person is describing, right, is that the stepfather got a prescription from a doctor for massive back surgery, correct?

A. Presumably, I am inferring -- I mean I only have the same information that is available to me, and it says that the stepfather had a massive back surgery. It doesn't say where he got

the opioid painkillers from, so I wouldn't --

Q. You can't infer that from "he would get it filled" --

A. Right. The information on the page does not describe where it is from.

Q. Okay. But do you think it is a fair inference that he was getting the prescription filled that was prescribed by a doctor for a massive back surgery?

MR. ARBITBLIT: Object to form.

A. I think that -- that could be a fair assumption. I just don't have any more information than you with regard to what is on this page.

Q. (BY MR. HERMAN:) Well, I am going to ask you to assume that his doctor prescribed the prescription opioids for his massive back surgery, intending that they would be used for a legitimate medical purpose of relieving his pain.

Okay. Do you understand what I am asking you to assume?

A. There are a lot of assumptions embedded in that question.

Q. Well -- I am asking -- I am asking you to assume. So, yes, there is an assumption that this person had a massive back surgery, and

his doctor prescribed him opioids, intending that they would be used for the legitimate medical purpose of relieving post-operative pain. Okay. You understand what I am asking you to assume?

MR. ARBITBLIT: Object to form. Incomplete hypothetical.

A. I generally understand the scenario. It is just -- it is not clear what opioids, how much -- I mean clearly there was such a surplus supply left over that -- I mean within the confines of this example.

Q. (BY MR. HERMAN:) That can happen, right? You have a number of studies that you cite in your report where doctors are prescribing things for things like C-sections, mastectomies, thoracic surgery, where the study is looking at how their prescription opioid pills are left over after surgery, correct?

MR. ARBITBLIT: Object to form.

A. There are studies that describe unused medication after -- that people received, that people don't use of their opioid medication.

Q. (BY MR. HERMAN:) Yeah, including -- you cite one that estimates there would be a hundred million prescription opioid pills left over

after dental surgeries per year, correct?
A. Which study is that?
Q. Well, do you not recall that study?
MR. ARBITBLIT: Object to form.
A. I just would -- I would prefer to see the study before testifying what it says.
Q. (BY MR. HERMAN:) Okay. We can come back to that. But going to my hypothetical here with -- assuming that the doctor wrote that prescription intending that it would be used by the patient to relieve pain for post-operative -- post-operative pain for a massive back surgery, do you think there would be anything wrong with a pharmacy filling that prescription?
MR. ARBITBLIT: Object to form. Incomplete hypothetical. Asked and answered.
A. My general understanding is that pharmacies have responsibilities in terms of dispensing medication that has been prescribed. And there's no information in this hypothetical scenario to know whether the pharmacy that dispensed this prescription that was then used by a twenty-five year old was dispensed responsibly.
Q. (BY MR. HERMAN:) Well, I am asking you to assume that it was dispensed pursuant to a

prescription for postoperative pain following a massive back surgery. Do you take issue with the pharmacy filling such a prescription written by an FDA -- by a licensed prescriber for an FDA-approved medication?

MR. ARBITBLIT: Object to form. Asked and answered. Incomplete hypothetical.

A. I have no information on whether the pharmacy fulfilled their responsibilities with regard to this particular prescription.

Q. (BY MR. HERMAN:) Okay. Let's assume -- let's assume that the prescription was written for a legitimate medical purpose for post-operative pain following a massive back surgery. Okay. I am asking you to assume that now.

MR. ARBITBLIT: There's no question pending.

Q. (BY MR. HERMAN:) And the pharmacy appropriately filled that prescription as a prescription written by a licensed medical provider for an FDA-approved medication for a legitimate -- prescribed for a legitimate medical purpose. So I am asking you to assume that the prescription was written appropriately and filled appropriately,

okay?

A. There's no information on whether there was a co-prescription with benzodiazepines. There's no information whether there were multiple prescriptions written and this person was getting it from multiple pharmacies, which also should be a responsibility of the pharmacist to check. So I can't answer that hypothetical without information on what other potential --

Q. I understand you don't want to answer the hypothetical that I am asking. But I'm asking a very specific hypothetical. It is a prescription written by a doctor for a legitimate medical purpose. You agree with me that a pharmacy can legally fill a prescription written by a licensed prescriber for an FDA-approved medication for a legitimate medical purpose, correct?

MR. ARBITBLIT: Object to form. Argumentative, badgering, incomplete hypothetical.

A. Is there a co-prescription with benzodiazepines in your hypothetical scenario?

Q. (BY MR. HERMAN:) Professor Keyes, I'm not trying to fight with you here. I am limiting it to a prescription opioid written for a legitimate medical purpose, appropriately filled by

the pharmacy. That is the hypothetical. Do you understand?

MR. ARBITBLIT: Object to form.

A. I understand the hypothetical, and it cannot be answered yes or no without additional information.

Q. (BY MR. HERMAN:) I haven't even asked my question. I am just asking you to assume appropriately written, appropriately filled. Got it?

MR. ARBITBLIT: Object to form.

Q. (BY MR. HERMAN:) Okay.

MR. ARBITBLIT: Assumes facts not in evidence. Incomplete hypothetical.

Q. (BY MR. HERMAN:) Now, what this person describes here is that the patient who received an appropriate medication did not properly store or dispose of the medication, correct?

MR. ARBITBLIT: Object to form. Assumes facts not in evidence. Incomplete hypothetical. Misstates the record.

Q. (BY MR. HERMAN:) Well, this description says the stepfather didn't really like the way they made him feel so they were just sitting, you know, sort of around the house. Do

you think that describes a scenario where prescription opioids were not appropriately disposed of or stored?

MR. ARBITBLIT: Objection. Incomplete hypothetical.

A. I don't know how they were stored in this hypothetical scenario. I only know what you know, that they were sitting around the house.

Q. (BY MR. HERMAN:) And that -- a pharmacy can't control whether a patient appropriately prescribed prescription opioids that are appropriately dispensed are just sitting around a house?

MR. ARBITBLIT: Objection. Incomplete hypothetical.

A. I would say a pharmacy can control whether the person received the opioid prescription in the first place. Certainly they are a part of that chain of receipt.

Q. (BY MR. HERMAN:) Sure. And here I have asked you to assume, following a massive back surgery, that these prescriptions were appropriately prescribed and appropriately filled. Everything is appropriate when they leave the pharmacy. Can the pharmacy control how the patient

stores prescription opioids?

MR. ARBITBLIT: Objection. Incomplete hypothetical.

A. Again, I -- the hypothetical scenario is asking -- has not established that the pharmacy did the appropriate responsibilities to ensure that this medication was being prescribed safely.

Q. (BY MR. HERMAN:) You are unwilling to accept what I am asking you to assume, that everything was appropriate with the prescription when it left the pharmacy. You are unwilling to accept what I am asking you to assume?

A. I -- I can engage in the -- in the hypothetical. I just --

Q. Well, I have been asking you to do that for a while.

MR. ARBITBLIT: Counsel, you have asked so many different hypotheticals, and now you are badgering. Some are based on the article and some are not. I will object. It is confusing and argumentative and badgering.

Q. (BY MR. HERMAN:) Well, do you agree with me that a pharmacist and a pharmacy cannot control how appropriately dispensed prescriptions are stored?

A. I would agree that once a prescription leaves the pharmacy, the pharmacy cannot monitor how it is stored.

Q. And can't control how it is disposed of?

A. That is right.

Q. Can't control whether the patient takes more than the doctor instructed the patient to take at one time?

MR. ARBITBLIT: Object to form.

A. Again, I do think the pharmacy has some responsibility in terms of ensuring that the prescriptions that are dispensed by the pharmacy are appropriately dispensed.

So -- I would not agree with that statement.

Q. (BY MR. HERMAN:) Yeah, again, I think -- I understand that you don't -- but I am asking you, prescriptions appropriately dispensed, you agree that after that point, a pharmacy and a pharmacist cannot control whether the patient takes the medication as prescribed?

THE REPORTER: Someone needs to mute themselves or I hear something in the background.

A. I don't think I would agree with that

as a blanket statement, given that the pharmacy has control over the number of pills that are dispensed.

Q. (BY MR. HERMAN:) Well, it is a doctor that decides on the amount and dosage in a prescription, correct?

MR. ARBITBLIT: Object to form. Misstates the evidence.

A. The -- the prescription is written for a specific amount and dosage.

Q. (BY MR. HERMAN:) Can I ask you to go to -- can I ask you to go to Page 19 of your report. And on Page 19, towards the bottom, you are discussing one of the studies. And you say, "Most problematically, the article reports on an overall association between any opioid use and opioid use disorder, but this association is uninformative and essentially pointless. It is well documented that risk of opioid use" -- opioid, sorry -- "well documented that risk of opioid-related adverse outcomes are heterogenous by dose and duration of use."

Do you see that?

A. I do.

Q. And I read that correctly?

A. Yes.

Q. And when you say that risk of opioid -- when you say, "risks of opioid adverse outcomes are heterogenous by dose and duration," you mean that the risk differs depending on the dose and duration that a patient takes, correct?

A. Yes.

Q. And then on Page 20, near the top of the page, you say, "This same issue underlines Cepeda, et al., which was also included in the Higgins review; the study includes data for almost forty thousand patients from insurance claims databases and reports an overall association between opioid prescriptions and claims-recorded opioid use disorder, without disaggregating the dose and duration. Such information is uninformative for assessment of opioid use disorder risk with prescription opioid use, given the known heterogeneity," correct? Did I read that correctly?

A. Yes.

Q. And what I understand you to be saying there, and correct me if I am wrong, is your view is that it is essentially pointless to give an association between opioid use and opioid use

disorder that doesn't recognize there will be differences in risk, depending on how one uses prescription opioids, correct?

A. That is not exactly what the report says. I think overall assessment of the relationship between opioid use and opioid use disorder do provide some information, but we know there's a dose response relationship between dose and duration and opioid use disorder and overdose. So it is, you know, important to evaluate that in an overall body of literature, to provide that information.

Q. Right. You have got to separate -- if you were to apply the risk from, for example, all acute users, you couldn't extrapolate that risk to all users, right? It is informative to -- by dose and duration, right? I'm sorry. I asked about four questions in there. But let me strike that and ask a different one.

But what you are saying is, when you are evaluating risk, there are different risks, depending on whether someone takes an acute dose or a high dose, correct?

MR. ARBITBLIT: Objection, vague.

A. It really depends on what the

research question is and what you are looking at. There are a number of ways to evaluate risk of opioid use disorder after opioid use. One way to evaluate it that is very informative is to see how different the risk is based on dose and duration. And the risk of opioid use disorder is much higher when you have high dose and high duration.

Q. (BY MR. HERMAN:) Yeah, but you couldn't -- it would be uninformative, to borrow your language, to use the risk percentage for acute users and apply that to long-term users, correct?

A. It would depend on the specific context in which someone was trying to make those extrapolations. I wouldn't want to make a blanket statement.

Q. But so do you -- let's say I took a population of all acute users and presumably came up with a relatively low percentage who developed OUD. It would be wrong for me to take that percentage and apply it to long-term users, correct?

MR. ARBITBLIT: Objection to the form.

A. I would need more information about the studies that you were trying to extrapolate

between.

Q. (BY MR. HERMAN:) Okay. Well, let's look at -- can I ask you to take out 7 -- CVS 7-18, which will be Exhibit --

MR. HERMAN: What are we up to now? 7-18 --

MR. ACTON: 7-18? 7-18?

MR. HERMAN: Yes.

MR. ACTON: 17.

MR. HERMAN: This is Exhibit 17, Professor Keyes. Do you have it?

(Exhibit 17 was marked for identification.)

A. I do.

Q. (BY MR. HERMAN:) And this is a study that discusses -- or that is titled "The Role of Opioid Prescriptions in Incident Opioid Abuse and Dependence Among Individuals with Chronic Non-Cancer Pain: The Role of Opioid Prescription"; is that correct?

A. Yes.

Q. And if you look at Page 3 under

Measures, Independent Variables. So this report looked at days of use. And so acute was defined -- or none would be zero. Acute was one to ninety days, or chronic was ninety-one plus days. Is that correct?

A. Yes.

Q. And then if you look at the next page, it also looked at dosage. And the average daily dose was measured in morphine equivalents and grouped as none (zero milligrams), low dose (one to 36 milligrams), medium dose (36 to 120 milligrams), and high dose (120 plus milligrams). Is that correct?

A. Yes.

Q. Okay. And if you look at Page 5 under Results, there were five hundred and sixty-eight thousand six hundred and forty individuals in this analytical sample; is that -- is that correct?

A. Yes.

Q. Okay. And is that a fairly large sample?

MR. ARBITBLIT: Object to form.

A. That is a large sample, yes.

Q. (BY MR. HERMAN:) And the majority of

the sample had no prescribed opioid use in the twelve months following the index date, correct?

A. 65.3 percent had no opioid use.

Q. A --

A. No prescribed opioid use.

Q. And thirty-five -- the flip side of that is approximately thirty-five percent of the sample received opioids?

A. Yes.

Q. And low dose acute and medium dose acute were the most common type of the opioid use?

A. Yes.

Q. 15.9 percent for low dose acute?

A. Yes.

Q. 14.7 percent for medium dose acute?

A. Yes.

Q. Okay. And high dose chronic use was the least common, 0.1 percent of the sample?

A. Yes.

Q. And then among the entire sample prescribed opioids, 94.5 percent were acute users?

MR. ARBITBLIT: Objection.

A. That is right.

Q. (BY MR. HERMAN:) And if you go down to the second paragraph, it says, "Among the total

sample, four hundred and ninety-seven (0.1 percent) had a new diagnosis of OUD in the post-index period." Did I read that correctly?

A. You read that correctly.

Q. And because such a large percentage of the sample is acute users, you wouldn't apply that 0.1 percent to chronic users, correct?

MR. ARBITBLIT: Object to form. Misstates the evidence.

MR. HERMAN: Well, I am asking.

Q. (BY MR. HERMAN:) Could I take that 0.1 --

MR. ARBITBLIT: Your .1 is to the whole sample. You are asking -- never mind. Sorry. Object to form. Misstates the evidence.

Q. (BY MR. HERMAN:) Could you take that 0.1 percent of new diagnosis of OUD and apply that to a population that included only chronic users and expect to get the same results?

MR. ARBITBLIT: Object to form. Misstates the evidence.

A. I don't -- what is the goal of the analysis in the hypothetical?

Q. (BY MR. HERMAN:) Well, I think I am trying to follow what you are saying in your

report, that something that just looks at a patient population and doesn't account for heterogeneity of dosage and duration wouldn't extrapolate to -- would be uninformative.

MR. ARBITBLIT: Object to form. Vague.

Q. (BY MR. HERMAN:) All right. Let's keep going.

A. I mean .1 percent is the total percentage of new OUD diagnosis in the total sample.

Q. (BY MR. HERMAN:) Okay. Let's just keep going.

Next down it says, "The unadjusted rates of post-index OUD diagnosis for the various opioid dose/days categories were 0.12 percent (111 out of 90,415) per low dose acute; 0.72 percent (50 out of 6,902) for low dose chronic; 0.12 percent (111 out of 83,542) for medium dose acute; 1.28 percent (47 out of 3,654) for medium dose chronic; 0.12 percent (15 out of 12,378) for high dose acute; and 6.1 percent (23 out of 378) for high dose chronic."

Was that the results of the unadjusted rates of post-index OUD diagnosis for

the various opioid dose/days categories that they found?

A. Yes.

Q. Do you know how many prescription opioid patients in Lake and Trumbull County fit into the category of acute patients?

A. No.

Q. Do you know how many prescription opioid users in Lake and Trumbull County were low dosage patients?

A. I am not aware.

Q. Do you know how many patients who fill prescriptions at CVS fit into each of the categories discussed in this report?

A. I don't.

Q. Would your answer be the same for Rite Aid, Giant Eagle, Walgreens and Walmart?

A. Yes.

Q. Besides dose and duration, there are other individual risk factors that matter -- that matter in terms of assessing risk to a particular patient, correct?

A. You mean risk for development of OUD?

Q. Yes. Yes.

A. So the question is whether there are

risk factors for OUD over and above dose and duration. That is the question?

Q. That is the question.

A. OUD -- dose and duration are the strongest risk factors for OUD development, but other risk factors include things like, you know, sex and previous history of psychiatric disorders and drug use and other -- kind of individual vulnerabilities.

Q. Okay. Sticking with your counsel's admonition, you have discussed different individual level risk factors in your previous testimony at deposition and the testimony you gave in New York, correct?

A. I believe so.

Q. And you have also discussed individual risk factors in articles that you have authored?

A. I have.

Q. Is there any reason that individual risk factors discussed in your previous testimony and articles would not apply to people in Lake County and Trumbull County?

MR. ARBITBLIT: Object to form.

A. The -- I would look at each risk

factor specifically, but in general the risk factors that have been identified in the literature, I would -- I would make the assumption that they would generally generalize to Lake and Trumbull County.

Q. (BY MR. HERMAN:) Sure. Like if something was a differentiation on urban versus rural and one of the counties wasn't rural or urban, it wouldn't apply. But generally they would apply, correct?

A. I would look at each one specifically, so I wouldn't want to make a blanket statement. But, you know, depending on which specific risk factors we are talking about, I could make a determination of generalizability.

Q. Okay. But the ones you mentioned, sex, mental health history, previous drug use, no reason to think that those wouldn't be risk factors for individuals in Lake and Trumbull County?

A. I don't have reason to think that they wouldn't be.

Q. Okay. And can I ask you to look at Page 11 of your report? And the last sentence where you say, "This framework does not preclude or ignore that addiction and related harms are

multi-factorial in their etiology." What is "multifactorial in their etiology"?

A. I'm not seeing on Page 11 --

Q. It is right above "Methodology For Review of the Evidence."

A. Okay. So the full sentence is "This framework does not preclude or ignore that addiction and related harms" --

THE REPORTER: I'm sorry. Slow down, please.

A. I'm sorry. Do you want to read the whole sentence?

Q. (BY MR. HERMAN:) Well, I am really just asking you a question in that sentence. But what is "multi-factorial in their etiology"?

A. That means that there can be multiple causal risk factors for an outcome.

Q. Okay. When you say a disease is multi-factorial, you mean that a single cause does not produce a disease but the combination of many causes produce a disease, correct?

MR. ARBITBLIT: Object to form.

A. Not necessarily.

Q. (BY MR. HERMAN:) That is not how you described multi-factorial in your textbook,

Epidemiology Matters?

A. It means that there can be multiple causal risk factors that simultaneously produce an outcome. Sometimes that can be multiple risk factors -- multiple causes interacting with each other. Cigarette smoking is a good example. Smoking is a cause of lung cancer, but not all smokers get lung cancer. So there have to be other factors too.

Q. Just sticking with dosage and duration abuse for a moment. In your report you cite the Jamison study as having the highest rates of addiction, correct? Do you recall that?

MR. ARBITBLIT: Object to form. Misstates.

A. I just want to find the -- I believe I am referring to a review article. I say the highest rate of addiction in the review article documented --

Q. (BY MR. HERMAN:) Fair enough. In bold, it is the highest in bold -- Jamison has the highest rates of addiction of study discussed in the Vowles article, correct?

A. Yes, the study where all patients were on long-term prescribed opioids for noncancer

pain.

Q. And as you say on Page 16, "Individuals in the study had been using opioids for an average of five to six years. 34.1 percent of the sample had evidence of opioid use disorder, including thirty-one percent of men and 36.7 of women, indicating a high level of opioid use disorder when patients are assessed with validated instruments as well as objective measures of the presence of opioids, such as urine toxicology," correct? That is the full sentence?

A. That is the full sentence.

Q. And so after using prescription opioids for an average of five to six years, approximately two-thirds of the patients did not exhibit an opioid use disorder?

A. A little less than that, thirty-four percent. So I guess that would be one hundred minus thirty-four percent.

Q. So approximately sixty-six percent, making --

A. Approximately.

Q. 65.9 percent?

A. Correct.

Q. Okay. So would you agree with me

that characteristics of opioid use, like dose and duration, can only tell you someone might be at risk for opioid use disorder?

MR. ARBITBLIT: Object to form.

A. No. I would not agree with that.

Q. (BY MR. HERMAN:) Well, if I told you that someone used opioids for five to six years, would you be able to tell me if that person was in the 65.9 percent who didn't develop a disorder or the 34.1 percent who did develop an opioid use disorder?

MR. ARBITBLIT: Object to form. Incomplete hypothetical.

A. So in this study, the 34.1 percent of people who had opioid use disorder were not at risk for opioid use disorder. They had opioid use disorder.

Q. (BY MR. HERMAN:) I'm asking --

A. So --

Q. Sorry. I didn't mean to cut you off. Please --

A. I don't understand the hypothetical.

Q. Well, I am asking you, in this study people who used opioids for five to six years, 34.1 percent developed an opioid use disorder, correct?

A. Yes.
Q. And so what you say with that is duration of use increases your risk for developing an opioid use disorder, right?
A. That is not a conclusion that I draw from this study. But from the body of evidence, yes, duration is a risk factor for opioid use disorder.
Q. Okay. But if a person -- if I told you a person had used opioids for five to six years, would you only be able to tell me that person had an increased use of developing an opioid use disorder as opposed to being able to tell me whether that person did, in fact, develop an opioid use disorder?
MR. ARBITBLIT: Objection, vague.
A. If I was given no additional information other than the duration of use, you could say what the probability is that they developed opioid use disorder, but no definitive, much like any risk factor.
Q. (BY MR. HERMAN:) And what additional information -- well, let me ask it this way: Well, what additional information would you need to be able to tell me if that person did, in fact,

develop an opioid use disorder?

A. In epidemiology we quantify things in terms of probabilities and risk factors. And so with additional information we could refine the probability and risk factor assessment.

Q. Okay. But to actually know whether the person developed an opioid use disorder, you would have to have a diagnosis code? What would you need?

MR. ARBITBLIT: Object to form, vague.

A. To know whether a person develops opioid use disorder, one would assess for opioid use disorder.

Q. (BY MR. HERMAN:) And you haven't looked at patient files for individuals in Lake or Trumbull County to see if any particular patient has an opioid use disorder diagnosis, correct?

A. No.

Q. Earlier today, I believe you testified that doctors -- you were troubled with the term "legitimate medical purpose" because you felt doctors did not have the right information about the risks and benefits of opioids at the time they made the prescription, correct?

A. I don't -- that is not a complete characterization of my testimony.

Q. Okay. Well, why don't we -- if I could ask you to open up Exhibit 4.

MR. HERMAN: But what is CVS 4 -- what exhibit are we on?

(Off-the-record discussion.)

Q. (BY MR. HERMAN:) This is going to be Exhibit 18.

(Exhibit 18 was marked for identification.)

Q. (BY MR. HERMAN:) This is a copy of the transcript of your testimony from your April 29th, 2019, deposition in the Cuyahoga and Summit County case?

A. Yes.

Q. And can I ask you to turn to Page 82? And if you look at Line 16, I asked you, "You would agree that a prescriber is only supposed to write prescriptions for legitimate medical reasons, correct?"

And you answered, "I think that prescribers are prescribing based on a set of information that they are given and that oftentimes the risk of opioids were" -- you said overstated

but you correct it later to understated, "the risk of prescription opioids were understated." So I think --

A. I'm sorry. I don't mean to interrupt you, but I just want to find the page.

Q. Oh, I'm sorry. I thought you were there.

A. No, I'm sorry. I was looking at the page at the bottom, not the page --

Q. Okay. I apologize.

A. I apologize.

Q. It is Page 22 of the overall.

A. I see. Okay. Sorry.

Q. So I asked you, "You would agree that a prescriber is only supposed to write prescriptions for legitimate medical reasons, correct?"

And you answered, "I think that prescribers are prescribing based on a set of information that they are given, and oftentimes that the risk of opioids were" -- and you corrected it later to understated, "the risk of prescription opioids were understated, and so I think that physicians are in a difficult position when they are trying to write prescriptions for legitimate

medical reasons."

Is that what I asked you and the answer you gave?

A. Yes.

Q. Okay. And one of the opinions, if you look at your report on Page 4, Opinion Number 4, the first sentence is, "Medical use of opioids is associated with the development of opioid use disorder at higher rates than were reported by drug manufacturers." Did I read that opinion correctly?

A. Yes.

Q. And is that what you were referring to in your testimony that we just looked at when you said the risks were understated?

MR. ARBITBLIT: Object to form.

A. Opioid use disorder is one of many risks of using an opioid. So I said the risks were understated, and one risk that was understated is the development of opioid use disorder.

Q. (BY MR. HERMAN:) Okay. What -- what other risks were understated?

A. Overdose is, you know, a pretty clear one. And I believe I cite another paper that goes through quite a few other medical conditions that are consequential to prescribed opioid use.

Q. Who understated the risk of overdose?
MR. ARBITBLIT: Object to form.
A. Who understated the risks of overdose?
Q. (BY MR. HERMAN:) Yes.
A. I'm not sure I --
Q. Well, you said the risks of overdose were understated, that that was one of the risks that was understated. So I was just asking who, who understated, if you know?
A. I think there certainly is evidence from drug manufacturers, and there may be other companies that also produce material that included information on the supposed safety of these medications that may not have been accurate.
Q. Sitting here today, the only one you are aware of, though, is drug manufacturers?
A. I am not offering opinions about specific companies' materials. I think there's sufficient evidence that, overall, various companies that sold and distributed opioids understated risks.
Q. Well, I -- Professor Keyes, I am sure in your professional life, you want to be pretty precise when you say things like that, that

companies, generally -- I'm just asking: Sitting here today, I'm not asking you for a specific. I asked you about a category, manufacturers.

Is that the only category you are aware of that understated the risks that you are speaking about?

MR. ARBITBLIT: Object to form.

A. I am not offering opinions about any specific companies at this time because I haven't evaluated those specific materials.

But I believe throughout the material that I have cited in this report, including the IOM report, including several other sources of material, there's sufficient evidence that a broad range of companies that sold opioids understated the risks.

Q. (BY MR. HERMAN:) Are you aware of any statement by pharmacists or pharmacies that understated the risks of prescription opioids, sitting here today?

MR. ARBITBLIT: Object to form.

A. I have not evaluated that specific material, and I am not offering an opinion on that.

Q. (BY MR. HERMAN:) And the concern you are expressing in the testimony we have looked at

was that doctors relied on what you -- what you believe to be an understatement of the risks of opioids, correct?

A. In this specific testimony?

Q. That is right.

A. I was referring to physicians, yes.

Q. And do you have any reason to believe that pharmacists had better information than doctors about the risks and benefits of prescription opioids?

MR. ARBITBLIT: Object to form.

A. I don't have any -- I haven't evaluated any material that would indicate that pharmacists had different information.

Q. (BY MR. HERMAN:) Do you fault pharmacists for filling prescriptions written by licensed doctors for FDA-approved medications that the prescriber intended would be used for legitimate medical purposes?

MR. ARBITBLIT: Object to form. Incomplete hypothetical.

A. My testimony would be that pharmacies have a responsibility to do -- to do what is required of them in order to dispense safely. And so in terms of what caused the opioid crisis, I

would certainly look at all of those distribution channels, including pharmacies.

Q. (BY MR. HERMAN:) What's the basis for your statement that pharmacies have a responsibility? Where did you gain that understanding?

A. I think it is well-known in terms of kind of opioid policy and epidemiology.

Q. What specifically are you pointing to for your assertion that pharmacies have -- as opposed to pharmacists, have an obligation when dispensing prescription medications?

MR. ARBITBLIT: Object to form.

A. I am pointing to my knowledge of epidemiology and opioid policy.

Q. (BY MR. HERMAN:) Well, what specifically are you pointing to other than something that -- like how did you gain that understanding?

MR. ARBITBLIT: Objective -- objection, vague. Asked and answered.

A. I gained understanding of epidemiology and opioid policy through my research and my expertise.

Q. (BY MR. HERMAN:) What specific

policy are you pointing to?

MR. ARBITBLIT: Objection, vague.

Q. (BY MR. HERMAN:) Sitting here today, can you point me to any document or law or regulation, any source that you are relying on for that statement that pharmacies, as opposed to pharmacists, have an obligation with regard to dispensing prescription opioids?

MR. ARBITBLIT: Objection, vague.

A. My general -- this comes from my general knowledge about opioid law, which varies across time and across states. And my general knowledge is that pharmacies and the people who work there have a responsibility to dispense responsibly.

Q. (BY MR. HERMAN:) What law specifically?

MR. ARBITBLIT: Object to form.

A. I think there are various regulations in various states that inform what pharmacies have a responsibility to do in order to dispense appropriately.

Q. (BY MR. HERMAN:) Have you ever written anything on the laws or regulations surrounding the practice of pharmacy?

A. I am certainly involved in a number of different opioid policy projects that include regulations that would include pharmacies in them.

Q. Have you ever written anything about --

THE REPORTER: I'm sorry. You garbled. "Have you ever written anything" --

Q. (BY MR. HERMAN:) Have you ever written anything evaluating the laws and regulations of a pharmacy in connection with dispensing of prescription opioids?

A. I have certainly written a lot about opioid policies, some of which covers pharmacies and some which do not, including information on prescription drug monitoring programs. I have written a number of articles about various prescription drug monitoring programs and how they differ by state. And so I would point to those articles as providing a basis for my expertise.

Q. Well, I mean I have read all your articles on opioids, and I don't recall any of them discussing the obligations of a pharmacy or pharmacist when dispensing prescription opioids.

MR. ARBITBLIT: Objection. There's no question pending.

Q. (BY MR. HERMAN:) Can you point me to a specific article?

A. There are two systematic reviews on prescription drug monitoring programs that cover basically all fifty states across the last fifteen years. And so those would be articles that I would point to that would include information and laws that would regulate pharmacies.

Q. Do you know if there's any law in Ohio that says a pharmacy, as opposed to the pharmacist, has to check the OARRS system?

MR. ARBITBLIT: Object to form. Calls for a legal conclusion.

A. Yeah. I don't have expertise on the particulars of the OARRS system and how it -- and I am not offering an opinion how that regulates pharmacies versus pharmacists.

Q. (BY MR. HERMAN:) Okay. Are you offering -- the only -- so far, the only obligation I have heard you talk about are prescription drug monitoring programs. Can you think of any others that you have written about?

MR. ARBITBLIT: Object to form.

A. Yes -- sorry, Don. I cut you off.

MR. ARBITBLIT: I said object to

form. Misstates the testimony.

A. I have written about a number of different opioid laws and policies and more broadly, drug laws and drug policies. That is one of my areas of expertise. So I have written about an extensive array of drug policies.

Q. (BY MR. HERMAN:) Okay. Well, going back to PDMPs, do you have an understanding of whether in Ohio, a pharmacist is required to check the OARRS system in all circumstances or every time a prescription opioid is dispensed?

MR. ARBITBLIT: Object to form. Calls for a legal conclusion.

A. I have a general understanding of the Ohio law, and my understanding is that there's some controversy around the circumstances in which the PDMP is required to be checked, which is why there is a lot of overprescribing.

Q. (BY MR. HERMAN:) Do you have an understanding of whether the obligations of when a pharmacist is supposed to check the PDMP have changed over time?

A. In Ohio?

Q. Yes.

A. Yes. My understanding is that there

have been some changes to those regulations.

Q. Do you have -- are you claiming expertise in the obligations of pharmacists with regard to the OARRS system and their obligations in connection with it?

A. My expertise is generally on opioid policy, although I am not offering a specific opinion about pharmacists and the OARRS system.

Q. Okay. Are you offering an opinion about pharmacies and the OARRS system?

MR. ARBITBLIT: Object to form.

A. I'm not offering -- sorry.

MR. ARBITBLIT: Objection, vague.

Q. (BY MR. HERMAN:) Go ahead.

A. I am offering opinions about PDMPs in general, but not on the OARRS system in particular.

Q. Are you offering opinions about a pharmacy's connection or obligations in connection with use of the OARRS system?

A. I'm not offering an opinion about that.

Q. Do you know if pharmacies, as opposed to pharmacists, have the ability to access the OARRS system?

A. I guess I don't know what you mean by

pharmacies, because they are comprised by people. I mean, pharmacies are buildings.

Q. Well, you testified -- excuse me if I am wrong, but I believe you testified earlier you were drawing a distinction and saying that both pharmacies and pharmacists had obligations in connection with dispensing opioids. Did I understand you correctly?

A. My testimony was that yes, pharmacies have obligations in terms of their responsibilities.

Q. Okay.

A. But --

Q. Go ahead. I'm sorry. Well, the only one I have heard you mention so far, and we will keep going, but is in connection with PDMP usage. So I am asking you, do pharmacies have obligations to check the OARRS system in Ohio in connection with dispensing prescription opioids?

MR. ARBITBLIT: Objection. Calls for a legal conclusion.

A. My general understanding of the regulation would indicate that they do. But that is based on my reading of it as an epidemiologist.

Q. (BY MR. HERMAN:) And you are

qualifying your reading as an epidemiologist because you don't have expertise in interpreting the laws surrounding the practice of pharmacy, correct?

MR. ARBITBLIT: Object to form.

A. I have expertise in analyzing data and in -- and included in that analysis of data has been developing a pretty strong understanding of opioid policies and how they differ.

That being said, I'm not a lawyer. And so I -- you know, my reading of it as an epidemiologist would seem to indicate that pharmacies do have a responsibility.

Q. (BY MR. HERMAN:) Okay. Do you know -- again, do you know if pharmacies, as opposed to pharmacists, can access the OARRS system?

A. The pharmacists that are in pharmacies can is my understanding.

Q. Okay. And do you know whether, again, whether a pharmacist, in connection with every prescription opioid dispensed, is obligated to check the OARRS system?

MR. ARBITBLIT: Objection. Asked and answered. Calls for a legal conclusion.

A. My understanding is that there is some -- that the regulations in Ohio are -- there's some -- that they are not always obligated to check.

Q. (BY MR. HERMAN:) And so we have talked about OARRS. What other specific obligations do you understand a pharmacy to have in connection with the dispensing of prescription opioids?

MR. ARBITBLIT: Objection, vague, compound.

A. I would say that my understanding is generally about, you know, understanding the warning label and the risks and benefits in order to properly instruct patients on the usage of the medication.

Q. (BY MR. HERMAN:) And is that an obligation that belongs to the pharmacy or the pharmacist?

A. Given that the pharmacist works in the pharmacy, I would say that both have a responsibility to provide adequate care to patients who attend -- who get their medications at the store.

Q. Okay. So the pharmacist, if I am

understanding you correctly, has an obligation, as you interpret it, to counsel the patient on the warning label, correct?

MR. ARBITBLIT: Objection. Misstates the record.

A. Yeah. I would just go back to my testimony is that my understanding generally is that pharmacies have a responsibility to instruct the patient about the proper usage and risks and benefits of the medication.

Q. (BY MR. HERMAN:) Okay. And the reason you are saying pharmacies -- I mean I am just trying to get this straight. You are saying that the pharmacists, because they work in the pharmacy and they should do that, you believe that the pharmacy has on obligation?

MR. ARBITBLIT: Object to form.

A. Yes.

Q. (BY MR. HERMAN:) And so the obligation that you are talking about that is for the pharmacy is sort of if the pharmacist doesn't fulfill his obligation, his or her obligation, you think that the pharmacy is responsible?

MR. ARBITBLIT: Object to form. Calls for a conclusion.

A. I don't -- this is not an opinion that I am offering in terms of the responsibility. I mean, hundreds of thousands of people are dead from an opioid crisis. And I think that, you know, the responsibility of that is enormous in terms of the toll that this epidemic has taken on the population.

And so looking at the various ways that this could have been prevented includes a very close look on pharmacies.

Q. (BY MR. HERMAN:) Okay. But you don't actually -- I mean -- okay. Have you -- but you have not taken a close look at -- well, let me strike that.

I think you just said that you are not offering opinion on the obligations of pharmacies and pharmacists; is that correct?

MR. ARBITBLIT: Object to form.

A. That is right.

Q. (BY MR. HERMAN:) And you don't actually -- well, I will leave it. All right. Strike that.

MR. HERMAN: Should we -- I think we have been going about maybe a little over an hour. Should we take a little bit of a break?

MR. ARBITBLIT: I think there's about fifty minutes left.

A. Sounds good.

MR. HERMAN: Okay. Well, why don't we just take a break. I will try to organize myself a little bit.

THE VIDEOGRAPHER: Stand by. We are now off the record. The time on the video monitor is 4:15.

(Whereupon, a break was had from 4:15 p.m. until 4:27 p.m. EDT)

THE VIDEOGRAPHER: Stand by. We are now on the record. The time on the video monitor is 4:27.

Q. (BY MR. HERMAN:) Professor Keyes, do you know what percentage of current heroin users were misusing opioids, prescription or illicit, ten years ago?

A. Of the current heroin users now, what proportion ten years ago were misusing or using prescription opioids, that is the question?

Q. Misusing.

A. I don't know of an analysis that has been performed on current heroin users.

Q. I ask you to turn to Page 54 of your

report.

(Pause.)

Q. (BY MR. HERMAN:) And what I understand, if you look at the bottom of the page -- well, I'm sorry. Let's start with 53. I apologize. And one of the things you do here is you are estimating the number of people with opioid use disorder in Lake and Trumbull County, correct?

A. Yes.

Q. And at the bottom of Page 53, you acknowledge that estimating the number of people with opioid use disorder is a challenge, given that there's no systematic way to count this population, correct?

A. Yes.

Q. And so what you did was you took the calculated overdose rate of 0.52 per one hundred persons from the Larney systematic review and then divided that overdose rate into the number of overdoses, correct?

Well, that may be -- that may be too simplistic because you made an adjustment for fentanyl. As to prescription, the proportion that you estimate to be prescription opioids, you use the 0.52 per one hundred person-years from the

Larney study?

A. No. The total number of opioid users, I don't think I include the number of prescription opioid users specifically in this calculation. So I took the total drug overdose deaths and divide it by several different estimates of death rates, one of them being 0.52 per hundred thousand.

Q. And the other one being 1.56, which is your adjustment for -- based on multiplying that 0.52 by three; is that correct?

A. That's correct.

Q. And on -- and the Larney study was examining the risk for all overdose deaths, regardless of the drug that caused the overdose, correct?

A. All drug poisoning deaths, yes.

Q. And so it wasn't limited to deaths caused by prescription opioids or opioids generally?

A. That's correct.

Q. And on Page 54 at the bottom, you write, "However, the application of the 0.52 per one hundred person-years estimate needs to be adjusted for the increase in death rate that

occurred after fentanyl adulteration." Correct?

A. Yes.

Q. Okay. And the reason for that is because fentanyl is more lethal. If you use the same rate, 0.52, you would overestimate the number of opioid use disorder cases in Lake and Trumbull County, correct?

A. That is right.

Q. And what you are trying to do is to account for the, as you write here, the increase that occurred after fentanyl adulteration, correct?

A. Yes.

MR. ARBITBLIT: Object to form.

Q. (BY MR. HERMAN:) And you placed the time period when fentanyl adulteration began to occur as 2013, correct?

A. Not exactly.

Q. You don't say in several places in your report that the adulteration of the heroin supply with illicit fentanyl began to occur in 2013?

A. I used 2013 as an interruption in the time series from 2011 to 2015 for the change in overdose death rates.

Q. Well, other places you used 2013,

right, like when you are calculating the role of fentanyl illicit versus illicit played in overdose deaths in your estimate, right? You used an average of all deaths before 2013, and you attribute that to prescription opioids, correct?

MR. ARBITBLIT: Object to form. Vague.

A. That is a different analysis.

Q. (BY MR. HERMAN:) Okay. But I stated your analysis correctly, right? You assume for purposes of calculating overdoses that all fentanyl, all 40.4 T-codes before 2013 were prescription opioids?

A. I took an average of the years prior to 2013 to estimate a constant number of fentanyl overdoses that were due to prescriptions. So it is not all. It is the average across those years.

Q. Well, average after 2013. But to create that average, you assumed that every death that was coded 40.4 before 2013 was a prescription opioid death, correct?

A. The average of those years is an estimate of the number of prescription opioid deaths.

Q. Okay.

A. I don't ever assume that --
Q. You don't think --
A. I don't --
Q. You don't think your overdose death calculations before 2013 treat all deaths coded as 40.4 as prescription opioid related?
MR. ARBITBLIT: Object to form.
A. I believe I have answered the question. The method is to take an average of those overdose deaths prior to 2013 as an estimate of the number of fentanyl cases per year that are due to prescription opioids. It makes no assumption about the total number of T40.4 deaths.
Q. (BY MR. HERMAN:) Well, what about -- and we can look at some of these later, but I understand that you apply that average going forward for 2013, '14, '15, you know, all the years that follow 2013. But -- 2013 or later. But for 2012, if a death is coded T40, you attribute that death to prescription opioids. You don't do that?
MR. ARBITBLIT: Object to form.
Q. (BY MR. HERMAN:) I see you shaking your head.
A. I think I have explained the methodology, but I will explain it again. You take

an average of the deaths per year divided by the number of years, and you use that average as your estimate of the number of cases of prescription opioid deaths. I don't make assumption about all T40.4 cases.

Q. Well, in 2009, there was a death that was coded T with a T-code 40.4. Did you attribute that death to prescription opioids, or did you treat it some other way?

MR. ARBITBLIT: Object to form.

A. Are you looking at the specific spreadsheet? I can walk through the specific spreadsheet. Because I have used those numbers for various calculations. I think there might be some confusion.

Q. (BY MR. HERMAN:) We will look at it in a second. I think I understand it, but hopefully we can get on the same page.

But with the multiplier, if I could ask you to -- you came up with your multiplier three by looking at the increased overdose deaths from 2011 to 2015, correct?

MR. ARBITBLIT: Object to form.

Q. (BY MR. HERMAN:) And that --

THE REPORTER: I didn't hear an

answer.

MR. HERMAN: Oh.

Q. (BY MR. HERMAN:) Professor --

A. Yes.

Q. And you would agree with me, or maybe not -- do you agree with me that the rise in fentanyl deaths really began 2013 and later?

MR. ARBITBLIT: Object to form.

A. There was an increase in 2013 nationally.

Q. (BY MR. HERMAN:) Okay.

A. That is a statement I would agree with.

Q. If you use a time period from 2011 to 2015 and fentanyl began to play an increasing role in overdoses in 2013, 2014, '15, '16 and it kept going up, the role fentanyl was playing in overdoses, wouldn't your multiplier, by using a period that predates the introduction of fentanyl, underestimate the opioid use disorder cases?

MR. ARBITBLIT: Object to form.

A. No. And I can explain why.

What we did was we weighted the denominator of the multiplier correction for the proportion of deaths for which synthetic opioids or

T40.4 was involved. So as the years went on in which there was an increasing number of T40.4 deaths contributing to the overall drug poisoning deaths, that is accounted for.

That is precisely why we used the methods that we did, was because those T40.4 deaths kept increasing. So that by 2018, 2019 when an increasing portion of the overdose deaths are T40.4 deaths, we are using that higher death rate weighted to all of those deaths.

Q. (BY MR. HERMAN:) But if your 1.56 rate, you multiplied -- you came up with your multiplier three by looking -- you multiplied the Larney number, 0.52, by three. And you came up with that three times multiplier by looking at the increase in deaths from 2011 to 2015, correct?

A. Yes.

Q. And if you looked at -- did you look at whether if you used a time period from, say, 2014 to 2019, that the multiplier should have been higher than three?

A. That would have been an inaccurate and flawed method. The reliability of my method is that it relies on a standard and time-tested epidemiological practice of using an interruption

in a time series. So to describe more simply, what the interruption is intended to estimate is the amount of change in the probability that you die of a drug overdose, given that fentanyl is involved, not the number of people who are using fentanyl. Right.

So if you use 2015 to 2019, you would very well capture the number of people using fentanyl, but that would be the wrong number to use. The right number to use is the interruption in the time series immediately prior and immediately after the change in the contamination of the drug supply.

So we use that three times number because it was the interruption in the time series and then weight it, each of the denominators for every single year by the total number of drug overdoses that involved T40.4 in order to exactly not fall into the methodological flaw that you are describing of conflating the number of people who use fentanyl with the probability that you die given that you use.

Q. Well, I think if you are using a period to account for the increased lethality of fentanyl that predates fentanyl becoming, you know,

becoming being adulterated into the drug supply, you don't agree with me that you would underestimate the lethality and the role fentanyl played in overdose deaths?

MR. ARBITBLIT: Object to form. Asked and answered.

A. Yeah, I can explain it again. I mean you really do need that pre-fentanyl period so you have a baseline, right. You need to know the probability -- the change in the probability of deaths given that you used fentanyl versus that you didn't use fentanyl. So you need a time period in which the majority of people using drugs weren't using fentanyl, right.

And so that -- if you have seen other kinds of interrupted time series models, which, again, are very standard in epidemiology, exactly to estimate these types of parameters, I need to know a single point of change. And so when you have this like sharp interruption in a time series, you wouldn't use the later dates to estimate the change in the risk, because that would, again, conflate the number of users with the lethality of deaths.

So the interruption of the time

series exactly gets at the quantity that we want to get at, which is not how many people are using fentanyl, but is what is the change in the probability of death, given that you use fentanyl compared that you don't use fentanyl, not how widespread is fentanyl use.

Q. (BY MR. HERMAN:) Well, can I ask you to look at Table 2? Actually, let's go to --

MR. HERMAN: Jason, can I ask you to pull up Exhibit 13?

MR. ACTON: Yes.

Q. (BY MR. HERMAN:) This is CVS for you, Professor Keyes, 13. One is -- I believe all the tabs are going to be in there. The way this material, your chart was sent to us was as an Excel spreadsheet, which we will put up on the screen, and then PDFs that followed each tab.

MR. HERMAN: Why don't we mark that as Exhibit -- what are we up to? -- Exhibit 19.

(Exhibit 19 was marked for identification.)

MR. HERMAN: And if we could mark -- are all the tabs part of one exhibit? Okay. Well, why don't we mark the PDFs as 19-A, B, C, D, E [sic].

(Exhibit 19-A was marked for identification.)
(Exhibit 19-B was marked for identification.)
(Exhibit 19-C was marked for identification.)
(Exhibit 19-D was marked for identification.)

Q. (BY MR. HERMAN:) And Dr. Keyes, I don't think -- we sent you the PDFs, but we didn't have a good way to send you the Excel spreadsheet with its separate tabs. So I think -- we will put that on the screen, but I think we can hopefully walk through it together.

A. Sure.

Q. And -- oh, I have it here. Okay. And the tabs that you and I were discussing earlier is Figure 7 and 14 where we were talking about the averaging of T40.

A. Yes.

Q. Okay. And just so the record may be a little clearer, T40.1 is heroin, correct?

A. Yes.

Q. And T40.2 refers to natural or semisynthetic opioids such as oxycodone or

hydrocodone?

A. Yes.

Q. Okay. And T40.3 refers to methadone?

A. Yes. Yes, I think it is -- I think the category is something that is a little bit broader than that in terms of what it is called.

Q. I thought I took it from your report. But we will -- whatever T40.3 is, it includes methadone?

A. It includes methadone.

Q. And T40.4 refers to synthetic opioids such as fentanyl, correct?

A. Correct.

Q. And the issue that you and I, maybe not clearly for the record, we are sort of discussing is that T40 doesn't distinguish between prescription fentanyl and illegal fentanyl, right?

A. T40.4.

Q. T40.4, yeah.

A. That's correct.

Q. And it also can include fentanyl analogs like carfentanil, for example, right?

A. Yes.

Q. Okay. And so what you were trying to do in the overdoses is come up with a calculation

of when fentanyl became a problem. More of a problem by your estimation post 2013 was what number that T40.4 dash should be attributed to prescription versus illicit fentanyl, correct?

A. That's correct.

Q. And the way you came up with that number was, if I understand it correctly, is you took -- I want to get my column right, but Column H, and for every year before 2012 -- and we will just use Trumbull County as an example -- where there was a number in Column H, you added those up and you divided it by the number of years for which there was a number, correct?

A. My -- do you -- I guess one procedural question. Am I allowed to write on this? Just because I -- it is hard to see and I kind of want to circle things. I am happy to turn it in --

Q. I think unlike when we did it last time, this isn't -- the exhibit with you I think is not the official exhibit. Someone should correct me if I am wrong, but if it would be helpful to you, I think you can write on it.

A. Yeah. It's just I don't have the column number, so I want to figure out -- when you

say Column H, it doesn't say Column H on mine. That is okay. I think I can figure it out. And just based on -- I just wanted to make sure it is okay if I write on this.

Q. Yeah. Can you see the one that says T40.2 minus T40.4 minus T40.2 -- and then it says "Deaths that only" --

A. Yeah.

Q. I think that is what I am referring to as Column H. And that is meant to capture overdose deaths that were only T40.4, correct?

A. Correct.

Q. And so my understanding is that you before 2012 or before 2013, so 2012 or earlier, when you estimated the number of RX deaths, you added the column that is RX opioids not including synthetics, so the one that was T40.2, T40.3, and you added that to Column H. So everything before 2012, you treated everything in -- that was a T40.4 death as attributable to an RX opioid death. Is that correct?

A. Not exactly -- everything that was a T40.4 death that didn't have an additional contributing cause of an additional T-code. So if it had, for example, T40.4 and T40.1 -- that is

heroin and fentanyl, for example -- that was not treated as a prescription fentanyl death.

Q. Okay. And that is what you did for the time period before 2012, or 2012 or earlier? And then for 2013 --

THE REPORTER: I didn't hear an answer.

MR. HERMAN: Oh, I'm sorry.

THE REPORTER: Question: And that is what you did the time period before 2012, or 2012 or earlier?

A. And I said that is right.

Q. (BY MR. HERMAN:) And after 2012, or 2013 and later, my understanding is what you did was -- let's just use Lake County, I think, because it will be easier. Lake County has NA for 1999 to 2005, right? Do you see that?

A. That is right. Yes.

Q. And so you didn't have a number to use. So my understanding is you took the number in Column H for 2006 to 2012. You added those all up and you divided by the number of years for which you had data to come up with an average, right?

A. Yep. Yes.

Q. And then you rounded that up.

Because I think the number for each of these is 2., I think, five something and one is 2.7 something. So you rounded that up to three, right?

A. Yes.

Q. And then carrying that forward, you treated for each year three of the T40.4 overdoses as directly attributable to prescription opioids, correct?

A. That is right.

Q. And I think there was one year -- there was one year where I believe that -- and it is in Lake County where it says, 2013, if you see Column H has zero in it --

A. Yes, I see that.

Q. And when you go over to Column J, which I understand to be directly attributable to prescription opioids, it looks like you still added three to the nineteen. Was it -- I'm just wondering whether that was an oversight or whether there is a reason why that would occur.

A. I would have to go back and look through my calculations to see what I actually did there, because I don't have the calculations on this spreadsheet and I can't see the column headings either.

Q. Yeah. Well, if there's zero T40.4 deaths in the data, would you agree with me that you shouldn't add three T40.4 deaths to that?

A. Not exactly. There's not zero T40.4 deaths in the data. That is the estimate of the number of T40.4 deaths that don't have an alternate contributing cause. So there are T40.4 deaths in the data. So to derive an estimate of the number of total T40.4 deaths that are attributable to prescription opioids doesn't necessarily preclude a year in which there are zero T40.4-only deaths from having deaths that were due to prescription fentanyl.

So I generally try in my epidemiological practice to keep my rationale and my methods really consistent so that I don't fall into kind of methodological errors like assuming that a year in which there was zero T40.4 deaths only to be no deaths attributable to prescription opioids.

But I would have to go back and look at the calculations to know for sure.

Q. Okay. So am I understanding you correctly that if, for example, anything listed in Column H was only coded for T40.4, it didn't have

potentially a T40.1 code as well?

A. Well, it is an estimate of that, because we can't directly estimate the number of T40.4-only deaths from the CDC WONDER. All we can do is estimate the total number of T40.2 plus T40.3 plus T40.4 and we subtract out the T40.2 and T40.3 to try to get an estimate of how many of those are T40.4 only. But that doesn't preclude all of the T40.4 deaths in that group.

Q. But did you exclude T40.1 from those, or is it possible that someone that had -- is it possible that -- let's just stick with 2013 -- that your column that has 19 in it, which is -- includes T40.2, T40.3 and T40.4, could that also include T40.1, or no, you excluded those?

MR. ARBITBLIT: Object to form.

A. It absolutely does. Because, as I am sure you know, there are -- there's no -- people can be prescribed fentanyl and be using heroin. So you would not want to subtract out heroin users from that group.

Q. (BY MR. HERMAN:) Okay. And the only thing you looked at are T-codes related to opioids, correct?

MR. ARBITBLIT: Object to form.

A. For which --

Q. (BY MR. HERMAN:) Well, for all this, this entire chart, right. It is only looking at T40.1, T40.2, T40.3 and T40.4, right?

A. This chart only includes those T-codes, yes.

Q. And it is possible that these individuals had T-codes for other substances like cocaine?

A. I didn't look at that.

Q. It is possible they had T-codes for -- well, you didn't look at whether they included T-codes for any nonopioid drugs?

A. Yes. I did not look at that, as it was not the purpose of this chart.

Q. Okay. And I just had a question about your Figure 13 as well. Where -- I apologize if I missed it in your report, but my understanding is you are applying the Ohio numbers to the Ohio HUD rate and Ohio POUD rate to Lake and Trumbull County to come up with your estimate; is that correct?

A. Just so I can get on the same page, we are looking at Figure 13, which is the number of individuals with opioid use disorder that are

directly attributable to prescription opioids. And you are looking at the spreadsheet over here. I guess it is not -- 13. -- 13-D is where I derive the numbers that go into Figure 13.

And part of that calculation includes the Ohio heroin use disorder and Ohio prescription opioid use disorder rate and their overlap, their estimated overlap.

Q. Okay. And so you used the Ohio numbers that you -- and where did you get those rates from?

A. Those were from the National Survey on Drug Use and Health.

Q. Well, and so are we talking about -- let's be clear. Are we talking about the 53.4 percent number, or is that the number you are discussing when you are talking about the rate that you got? Or are you talking about --

A. That is different.

Q. Okay. Which rate -- can you give me a number, just to orient me? Because I think --

A. So in Exhibit CVS 13-D --

Q. Uh-huh.

A. -- on the top box, we have the total number -- so let's just take 2015 as an example.

Q. Yep.
A. There's the total number of OUD cases, which is estimated using that multiplier method that we went through.
Q. Yep.
A. And we have the total population size.
Q. Uh-huh.
A. The methodology used to estimate what proportion of those OUD cases are directly attributable to prescription opioids involves looking at the percentage of heroin use disorder and prescription opioid use disorder and their overlap, and using those percentages to derive the number that are directly attributable to prescription opioids.
Q. Okay. And you are using the Ohio rate, which I think you told me you got from the National Drug Use Survey?
A. National Survey on Drug Use and Health.
Q. Okay. All right.
MR. HERMAN: Well, if you give me five minutes, I may be done.
THE VIDEOGRAPHER: Stand by. We are

now off the record. The time on the video monitor is 5:01.

(Off-the-record discussion.)

(Whereupon, a break was had from 5:01 p.m. until 5:11 p.m. EDT)

THE VIDEOGRAPHER: We are now on the record. The time on the video monitor is 5:11.

Q. (BY MR. HERMAN:) Dr. Keyes, can I ask you to go to Page 24 of your report. I just want to touch on something we touched on earlier, but I didn't have the articles handy.

On Page 24 of your report, under the first bold heading, do you see where you say, "Available estimates indicate that ninety percent of patients prescribed opioids after surgery have unused medications, most of which are not disposed of or stored properly -- or stored safely"?

A. Stored safely.

Q. Okay. And if I could ask you to take out -- this was a study I mentioned earlier -- what is CVS 7-17 for -- in your folder. And this is going to be Exhibit 20 for the deposition.

(Exhibit 20 was marked for identification.)

Q. (BY MR. HERMAN:) Do you have that,

Professor Keyes?

A. I do. I do.

Q. And this is an article that I referenced earlier titled "Unused Opioid Analgesics and Drug Disposal Following Outpatient Dental Surgery: A Randomized Controlled Study [sic]." Do you see that?

A. I do.

Q. And this is one of the articles you cite in support of your statement that available estimates indicate that ninety percent of patients prescribed opioids after surgery have unused medication, correct?

A. Yes.

Q. Page 79, the reference is 79 in your report.

A. Yes.

Q. And if I could ask you to go to Page 2 and the first column, the fourth paragraph down. And do you see where it says, "The primary aim of this study was to describe patterns of opioid prescribing and consumption after dental surgery with a specific focus on measuring the quantity of opioids left unused"?

A. Yes, I see that.

Q. Okay. And if you go to the next page under the heading 3.1, do you see that in this study, they found that most patients, ninety-four percent, received a prescription for an opioid containing analgesic after tooth extraction?

A. I do.

Q. So at least in this study, ninety-four percent of patients got a prescription opioid -- prescription written for them after a tooth extraction, correct?

A. Yes.

Q. And if you go to Page 5, Section 4.1, and do you see where it says, "We found that fifty-four percent of opioid pills prescribed to a patient in this study (excluding those with dry socket) were left unused after surgery. Based on the national volume of surgical tooth extractions and literature on dental practitioners' prescribing practices, our results suggest that more than a hundred million opioid analgesic pills are left unused following surgical tooth extraction in the United States every year."

A. Yes. I see that.

Q. Okay. So earlier I asked if there was an article that suggested that there were more

than a hundred million opioid analgesic pills that are left unused following surgical tooth extractions in the United States each year. Is that what this article says?

A. Well, they don't calculate that -- I mean they haven't done a primary data analysis on that one hundred million opioid analgesic pills. They are extrapolating about a hundred million opioid analgesic pills if you assume that fifty-four percent of opioid pills in this sample that were unused can be mapped accurately onto the national volume of tooth extractions.

Q. Do you take issue with their analysis not involving a primary data review?

A. I think that their analysis is fine. What I would be cautious about is interpreting this study as showing that there's a hundred million opioid analgesic pills unused, because that is not what they are purporting to do.

Q. Okay. Well, they do say that their results suggest that there are a hundred million unused opioid pills following tooth extractions in the United States per year, right?

MR. ARBITBLIT: Object to form.

A. The study states, "Our result

suggests that more than one hundred million opioid analgesic pills are left unused following tooth extractions in the United States." That is what the text says.

Q. (BY MR. HERMAN:) And I guess I am not understanding. What issue are you taking with that extrapolation?

A. I don't take an issue with their extrapolation. I would not conclude from this that this conclusively demonstrates that there are one hundred million unused pills. That is an estimate from this study.

Q. Okay.

A. So if you say studies have shown that there's a hundred million unused pills, that is not what the study shows nor is it -- it is not claiming to show that.

Q. I think I understand. They are making an estimate that is extrapolation. But to actually know whether there were really a hundred million pills left over, you would have to do additional primary data analysis; is that right?

MR. ARBITBLIT: Object to form.

A. Additional analyses would need to be done in order to conclude that this -- you would

have to do a study to -- that would provide rigorous analysis to conclude that there are a hundred million unused pills. That is not what this study was trying to show.

Q. (BY MR. HERMAN:) Okay. But -- all right. And if you go down, though, the next paragraph, it is, "these results are consistent with prior research regarding opioid use among post-surgical patients. Bates surveyed patients following urological surgery and found that forty-two percent of prescribed opioids remained unused two to four weeks after the procedure. Harris found that fifty-nine percent of opioids prescribed following outpatient dermatological surgery were left unused, and Rogers identified that sixty-six percent of opioids were unused among patients following outpatient orthopedic surgery."

And so it is discussing a number of studies that have found that prescription opioids are left over from prescriptions doctors write to their patients, correct?

MR. ARBITBLIT: Object to form.

A. These studies show that there's a large proportion of opioids that are unused.

Q. (BY MR. HERMAN:) And if you go to

the conclusion -- and this is, I believe, a study that was written in 2016, correct?

A. The data are from a randomized control trial that was conducted in 2015.

Q. And this study was published in 2016?

A. It was published in 2016.

Q. And dentists -- and if you go to the Conclusion, it says, "Dentists and oral surgeons could substantially reduce the amount of prescription opioids available for diversion by reducing the quantity of opioids prescribed following these procedures. Recently-published recommendations in the dental literature highlight this opportunity," right?

A. Yes, that is what that says.

Q. And would you agree with me that the studies that you cite on unused prescription opioids -- there are, I believe, three of them here -- that they are directed to trying to change prescriber behavior and the amount of opioids that they prescribe to patients following various surgical procedures?

A. No. The next sentence of this paper says, "The availability of a pharmacy-based drug disposal program with a financial incentive to

return unused opioid analgesics is associated with a lower rate of patients indicating that they planned to keep their leftover opioid pills."

So I think, at least with this paper, they are suggesting multiple points of intervention to reduce opioid -- unused opioid pills, some at the pharmacy level and some at the provider level.

Q. So they are suggesting, one, that prescribers reduce the number of prescription opioids that they prescribe for dental surgery, correct?

A. That is one intervention that is recommended.

Q. And two, they are suggesting that there are potentially pharmacy-based drug disposal programs with a financial incentive to get the patients to bring back unused prescription opioids, correct?

A. That is another intervention that is recommended in this paper.

Q. And do you agree that the other two studies that you cite about unused prescription opioids following surgical procedures are directed at changing prescriber behavior in the prescriptions that they write?

MR. ARBITBLIT: Object to form.

A. I would not agree with that without reviewing the articles.

Q. (BY MR. HERMAN:) Well, do you recall that one of them discusses finding the ideal number, and it estimates a number that would satisfy eighty percent of the patient's pain needs?

MR. ARBITBLIT: Object to form.

A. I would need to look at the article.

Q. (BY MR. HERMAN:) Why don't we do that.

MR. HERMAN: If I could ask you, Jason, to pull up seven --

Q. (BY MR. HERMAN:) Professor Keyes, if you could get out 7-16, 7-16.

(Exhibit 21 was marked for identification.)

MR. HERMAN: And this will be Exhibit 21.

Q. (BY MR. HERMAN:) Dr. Keyes, do you have that?

A. I do.

Q. And this is called -- this article is titled "Wide Variation in Excessive Dosage of Opiate Prescriptions for Common General Surgical

Procedures," correct?

A. Yes.

Q. Okay. And this is an article that was published in 2017, correct?

A. Yes.

Q. Okay. It is one you cite in your report?

A. I do.

Q. Okay. And can I get you to look at the first page, 709, second column, the last paragraph. Do you see where it says, "Providers both have societal imperative to avoid overprescribing and an obligation to ensure their patient's post-operative pain is addressed"? Do you see that text?

A. I do.

Q. And does that refresh your recollection that this paper, and we can go through more of it, is trying to address overprescribing by doctors balanced against the need to address post-operative pain?

A. That is not my read of the purpose of the paper. In the background section of the abstract, they talk about diversion as a major contributor to mortality. And while the

introduction focuses -- one paragraph of the introduction focuses on providers, other paragraphs focus on other --

Q. And what they are trying to do is to get prescribers to write less opioid prescriptions so there's less opportunity for pills left over after surgery to be diverted, correct?

A. That is not what their conclusion is or their objective as stated.

Q. That is not your understanding? All right. Well, let's keep going.

So under Methods, they "evaluated the five most common outpatient general surgery procedures performed at our academic medical facility in 2019. These were partial mastectomies, partial mastectomies sentinel lymph node biopsy, laparoscopic" -- I can't pronounce that word, but "cholecystectomy, laparoscopic inguinal hernia repair and open inguinal hernia repair," right?

A. Yes.

Q. And if you look at the next column over up at the very top, they found that in 2015 for those five procedures, 581 (90.5 percent) patients were prescribed an opioid, right?

A. Correct.

Q. And if you go down to the last paragraph, they obtained phone survey data on prescription opioid pills actually taken for a hundred and twenty-seven of those patients. Is that right?

A. That's right.

Q. And what they found was that a total of three thousand five hundred and forty-five pills were prescribed to those one hundred twenty-seven patients and that two thousand five hundred and twenty-seven, 71.3 percent, excess pills were prescribed, right?

A. Uh --

Q. If you look at the last sentence on Page 7 tab.

A. I see. I see. Two thousand five hundred and twenty-seven excess pills.

Q. And then if you go to Page 711, do you see in the second paragraph it says, "We calculate an ideal number of pills to prescribe for each operation by determining the number of pills that would satisfy approximately eighty percent of patients' post-operative opioid use"?

Do you see that?

A. I do.

MR. ARBITBLIT: I think we are out of time.

MR. HERMAN: Are we out of time?

MR. ARBITBLIT: Five hours, we are done.

MR. HERMAN: Okay.

THE VIDEOGRAPHER: Off the record?

MR. HERMAN: Thank you.

THE VIDEOGRAPHER: Stand by. You are now off the record. The time on the video monitor is 5:28.

(Deposition concluded at 5:28 p.m. EDT)

FURTHER THE DEPONENT SAITH NOT

C E R T I F I C A T E

STATE OF ALABAMA
JEFFERSON COUNTY

I hereby certify that the above and foregoing deposition was taken down by me in stenotypy, and the questions and answers thereto were reduced to typewriting under my supervision, and that the foregoing represents a true and correct transcript of the deposition given by said witness upon said hearing, to the best of my ability.

I further certify that I am neither of counsel nor of kin to the parties to the action, nor am I in anywise interested in the result of said cause.

/s/ LAURA H. NICHOLS
Commissioner-Notary Public, State of AL
ACCR License No. 3, Exp. 9/30/2021
GA CCR No. 2714, Exp. 4/1/2022
TN LCR No. 679, Exp. 6/30/2021
Transcript Certified on 6/3/2021

Veritext Legal Solutions
1100 Superior Ave
Suite 1820
Cleveland, Ohio 44114
Phone: 216-523-1313

June 4, 2021

To: MR. ARBITBLIT

Case Name: National Prescription Opiate Litigation - Track 3 v.

Veritext Reference Number: 4621640

Witness: Katherine Keyes , Ph.D. Deposition Date: 6/3/2021

Dear Sir/Madam:

Enclosed please find a deposition transcript. Please have the witness review the transcript and note any changes or corrections on the included errata sheet, indicating the page, line number, change, and the reason for the change. Have the witness' signature notarized and forward the completed page(s) back to us at the Production address shown above, or email to production-midwest@veritext.com.

If the errata is not returned within thirty days of your receipt of this letter, the reading and signing will be deemed waived.

Sincerely,
Production Department

NO NOTARY REQUIRED IN CA

DEPOSITION REVIEW
CERTIFICATION OF WITNESS

ASSIGNMENT REFERENCE NO: 4621640
CASE NAME: National Prescription Opiate Litigation - Track 3 v.
DATE OF DEPOSITION: 6/3/2021
WITNESS' NAME: Katherine Keyes , Ph.D.
In accordance with the Rules of Civil Procedure, I have read the entire transcript of my testimony or it has been read to me.
I have made no changes to the testimony as transcribed by the court reporter.

_____ _____
Date Katherine Keyes , Ph.D.
Sworn to and subscribed before me, a Notary Public in and for the State and County, the referenced witness did personally appear and acknowledge that:

They have read the transcript;
They signed the foregoing Sworn Statement; and
Their execution of this Statement is of their free act and deed.

I have affixed my name and official seal

this _____ day of_____, 20____.

_____
Notary Public
_____
Commission Expiration Date

DEPOSITION REVIEW
CERTIFICATION OF WITNESS

ASSIGNMENT REFERENCE NO: 4621640
CASE NAME: National Prescription Opiate Litigation - Track 3 v.
DATE OF DEPOSITION: 6/3/2021
WITNESS' NAME: Katherine Keyes , Ph.D.

In accordance with the Rules of Civil Procedure, I have read the entire transcript of my testimony or it has been read to me.

I have listed my changes on the attached Errata Sheet, listing page and line numbers as well as the reason(s) for the change(s).

I request that these changes be entered as part of the record of my testimony.

I have executed the Errata Sheet, as well as this Certificate, and request and authorize that both be appended to the transcript of my testimony and be incorporated therein.

_____ _____
Date Katherine Keyes , Ph.D.

Sworn to and subscribed before me, a Notary Public in and for the State and County, the referenced witness did personally appear and acknowledge that:

They have read the transcript;
They have listed all of their corrections in the appended Errata Sheet;
They signed the foregoing Sworn Statement; and
Their execution of this Statement is of their free act and deed.

I have affixed my name and official seal this _____ day of_____, 20____.

_____
Notary Public

_____
Commission Expiration Date

ERRATA SHEET

VERITEXT LEGAL SOLUTIONS MIDWEST

ASSIGNMENT NO: 4621640

PAGE/LINE(S) / CHANGE /REASON

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____ _____

Date Katherine Keyes , Ph.D.

SUBSCRIBED AND SWORN TO BEFORE ME THIS _____

DAY OF _____, 20_____ .

_____

Notary Public

_____

Commission Expiration Date

g

m

n

q

Federal Rules of Civil Procedure

Rule 30

(e) Review By the Witness; Changes.

(1) Review; Statement of Changes. On request by the deponent or a party before the deposition is completed, the deponent must be allowed 30 days after being notified by the officer that the transcript or recording is available in which:

(A) to review the transcript or recording; and

(B) if there are changes in form or substance, to sign a statement listing the changes and the reasons for making them.

(2) Changes Indicated in the Officer's Certificate. The officer must note in the certificate prescribed by Rule 30(f)(1) whether a review was requested and, if so, must attach any changes the deponent makes during the 30-day period.

DISCLAIMER: THE FOREGOING FEDERAL PROCEDURE RULES ARE PROVIDED FOR INFORMATIONAL PURPOSES ONLY. THE ABOVE RULES ARE CURRENT AS OF APRIL 1, 2019. PLEASE REFER TO THE APPLICABLE FEDERAL RULES OF CIVIL PROCEDURE FOR UP-TO-DATE INFORMATION.

VERITEXT LEGAL SOLUTIONS
COMPANY CERTIFICATE AND DISCLOSURE STATEMENT

Veritext Legal Solutions represents that the foregoing transcript is a true, correct and complete transcript of the colloquies, questions and answers as submitted by the court reporter. Veritext Legal Solutions further represents that the attached exhibits, if any, are true, correct and complete documents as submitted by the court reporter and/or attorneys in relation to this deposition and that the documents were processed in accordance with our litigation support and production standards.

Veritext Legal Solutions is committed to maintaining the confidentiality of client and witness information, in accordance with the regulations promulgated under the Health Insurance Portability and Accountability Act (HIPAA), as amended with respect to protected health information and the Gramm-Leach-Bliley Act, as amended, with respect to Personally Identifiable Information (PII). Physical transcripts and exhibits are managed under strict facility and personnel access controls. Electronic files of documents are stored in encrypted form and are transmitted in an encrypted fashion to authenticated parties who are permitted to access the material. Our data is hosted in a Tier 4 SSAE 16 certified facility.

Veritext Legal Solutions complies with all federal and State regulations with respect to the provision of court reporting services, and maintains its neutrality and independence regardless of relationship or the financial outcome of any litigation. Veritext requires adherence to the foregoing professional and ethical standards from all of its subcontractors in their independent contractor agreements.

Inquiries about Veritext Legal Solutions' confidentiality and security policies and practices should be directed to Veritext's Client Services Associates indicated on the cover of this document or at www.veritext.com.